THE 5TH INTERNATIONAL CONGRES ON

BIOMEDICINE

10TH - 19TH NOVEMBER 2021 - OFFLINE (VIRTUAL CONGRESS)

Medical Genetics

Medical Nano-Bio Technology

Microbiology & Infectious Diseases

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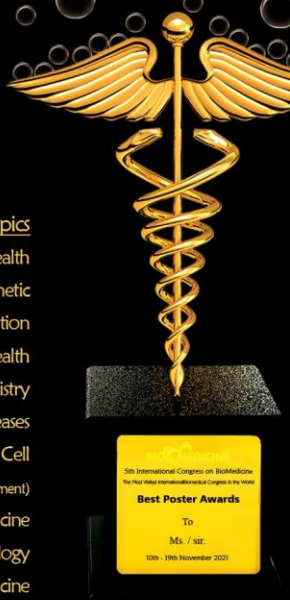
Women & Reproductive Health

Cancer

Geriatric Medicine

Tissue Engineening & Stem Cell



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- Health and Nutrition
- Social Health
- Medical Biochemistry
- Microbiology and Infectious Diseases
- Tissue Engineening and Stem Cell
- Cancer (Prevention-Diagnosis and Treatment)
- Personalized Medicine
- Medical Nano-Bio Technology
- Geriatric Medicine

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1. **Antitumor evaluation of mutant type of interleukin 2 in comparison to wild type IL-2 (Research Paper)**

Rada Dehghan,[1,*] Arezoo Beig Parikhani,[2] Yeganeh Talebkhan,[3] Mohammad Ali Shokrgozar,[4] Reza Ahangari Cohan,[5] Mahdi Behdani,[6]

1. Venom and Biotherapeutics Molecules Laboratory, Department of Biotechnology, Biotechnology Research Center, Pasteur Institute of Iran, Tehran, Iran.
2. Venom and Biotherapeutics Molecules Laboratory, Department of Biotechnology, Biotechnology Research Center, Pasteur Institute of Iran, Tehran, Iran.
3. Department of Biotechnology, Biotechnology Research Center, Pasteur Institute of Iran, Tehran, Iran.
4. National Cell Bank of Iran, Pasteur Institute of Iran, Tehran, Iran
5. Department of Nanobiotechnology, New Technologies Research Group, Pasteur Institute of Iran, Tehran, Iran.
6. Venom and Biotherapeutics Molecules Laboratory, Department of Biotechnology, Biotechnology Research Center, Pasteur Institute of Iran, Tehran, Iran.

Introduction: Interleukin-2 (IL-2), a member of the γ-chain cytokines with a molecular weight of 15kDa compromising of 133 amino acids and four alpha-helices, has been considered as an important cytokine in the survival, expansion, and function of CD8+ regulatory T cells, and natural killer cells in immunotherapy and treatment of melanoma and renal cell carcinomas. IL-2 is generally produced by CD4+ cells to activate CD8+ T and NK cells. It plays a crucial role in the induction of both cellular and humoral immunity through proliferation and activation of antigen-activated T cells, stimulation of NK cells, and homeostasis. Aldesleukin (Proleukin®) is known as one of the first FDA-approved cytokines in immunotherapy of metastatic renal cell carcinoma and malignant melanoma. However low efficacy of IL-2 therapy in cancer patients is due to the short serum half-life which causes administration of higher doses of IL-2 (720,000 IU/kg) and consequently, severe toxicity and vascular leak syndrome will occur. In addition, the interaction of IL-2with its alpha receptor and expansion of regulatory T (Treg) cells will activate immunosuppressive responses and reduces T cell-mediated anti-tumor activities.

Methods: mutated human IL-2 with a reduced affinity towards high-affinity IL-2Rα (CD25) was designed by selective amino acid substitutions. The amino acid sequence of the wild IL-2 and mutant IL-2 protein were separately subcloned into the pET28a expression vector. BL21 (DE3) E. coli strain was transformed with recombinant vectors. The expression of wild and mutant hIL-2 proteins was induced with 0.5mM isopropyl β-D-1-thiogalactoside (IPTG) at OD600nm and incubated for 6 hours. After purification on Ni–NTA agarose

column (ABT) at a flow rate of 1ml/min. Protein concentration was determined by UV adsorption at 280nm using a spectrophotometer. The purity of the eluted protein was analyzed on 12% sodium dodecyl sulfate-polyacrylamide gels electrophoresis (SDS-PAGE) and Coomassie Brilliant Blue staining. For western blotting, proteins were transferred to a nitrocellulose membrane. The membrane was treated with HRP-conjugated anti-His antibody and the protein bands were visualized using 3,3 diaminobenzidine tetrahydrochloride (DAB) solution as the substrate. We investigated the antitumor efficacy and cytotoxicity of the designed human IL-2 mutant rather than wild-type IL-2 (wtIL-2). Furthermore, we investigated the antitumor efficacy and cytotoxicity of the designed human IL-2 mutant rather than wtIL-2. Fifteen female C57BL/6J mice (6-8 weeks, 20g) were purchased from the animal resource center (Pasteur Institute of Iran) and maintained under standard housing conditions. TC1 cell line (mouse tumor cell line) cultured in DMEM medium supplemented with 10% FBS at 37°C under 5% CO2 atmosphere. On day 0, 1×106 cells in PBS (pH7.4) were injected subcutaneously (s.c) into the right flank of mice, and tumor growth was daily examined till the tumor dimension reached to 50 mm. After scarification of the animals, solid tumor samples were thinly sliced (2 mm thick) and subcutaneously transplanted into the shaved right flank of 15 mice which were divided into three groups (5 mice per group). Mutant and wild-type groups received recombinant purified IL-2 proteins which were diluted in sterile PBS (pH7.4) to a final concentration of 1 mg/kg was injected at the site of the tumor, two times per week for 1 month. The control group received 200µl PBS. Tumor size in each group was measured using a caliper and tumor volume was calculated.

Results: To evaluate the antitumor activity of the expressed IL-2 proteins, tumor-bearing C57BL/6 mice were treated with 1mg/kg of wild and mutant forms of IL-2 protein. The tumor size was measured for approximately 1 month after tumor transplantation and tumor volume was calculated. It was observed that tumor growth in animals treated with wild or mutant IL-2 proteins was significantly inhibited compared to the PBS treated control mice. Observations revealed that tumor volume of the mutant IL-2-treated mice was significantly decreased in comparison with the wild IL-2 treated group.

Conclusion: In accordance with the previous studies, it was found that reducing the interaction of IL-2 with its alpha receptor increases in vivo antitumor activity of this cytokine. Therefore, it seems that mutant IL-2 can be a promising agent for the treatment of cancer since it does not show the main side effects of IL-2-based immunotherapy.

Keywords: Interleukin-2, antitumor, regulatory T cells.

Study of anti-cancer effects of Grandivittin on the apoptosis pathway in A549 cell line (Research Paper)

Fateme Zomorodi Anbaji,[1,*] Seyed Jalal Zargar,[2]

1. Department of Cell and Molecular Biology, School of Biology, College of Science, University of Tehran, Tehran, Iran
2. Department of Cell and Molecular Biology, School of Biology, College of Science, University of Tehran, Tehran, Iran

Introduction: Homeostasis is maintained in normal tissues by a highly regulated process of cell proliferation. If there is an imbalance in the cell proliferation stage and the cell death stage, cancer develops. Lung cancer is the second most common cancer in men and women and the leading cause of death among cancers. The A549 cell line belongs to non-small cell lung cancer, accounting for 85% of all lung cancers. Grandivittin is one of the Dihydrofuran coumarins. Dihydrofuran Coumarins are a group of Coumarins that are very active as anti-cancer and cancer preventers. It also has various effects, such as antioxidant and laxative effects. This study investigated the effects of different concentrations of Grandivittin on cell survival and death in the A549 lung cancer cell line. The results of this study show the impact of Grandivittine on the inhibition of A549 cancer cells. This study found that in the A549 cell line, the rate of cell death increased at 24 and 48 hours due to increasing concentrations of 1.3, 1, 0.7, 0.4, and 0.1 GRD. By performing MTT tests at a concentration of 0.7 in 48 hours, we reached 50% lethality and confirmed this result by flow cytometry test. We performed a real-time RT-PCR test to evaluate the function of Grandivitin on the expression of genes affecting apoptosis. During these experiments, we observed that BAX, TP53, CASP9, and CASP3 genes had a significant increase in mRNA level, and the BCL2 gene also had a decrease in mRNA expression. Based on the results obtained in this study, Grandivittin can be a promising substance for the treatment of cancer that needs further research.

Methods: Cell line A549 was treated under the effects of incremental concentrations of 1.3, 1, 0.7, 0.4 and 0.1 µl Grandivitin at times 24 and 48 hours after culture and passage. Then RNA was extracted, and cDNA was made. By performing MTT tests at a concentration of 0.7 in 48 hours, we reached 50% lethality and confirmed this result by flow cytometry test. We performed a real-time RT-PCR test to evaluate the function of Grandivittin on the expression of genes affecting apoptosis.

Results: In this study, we observed that at a concentration of 50% lethality, 0.7 µl, in 48 hours, BAX, TP53, CASP9, and CASP3 genes had a significant increase in mRNA level, and the BCL2 gene also decreased mRNA expression.

Conclusion: Our study shows that grandivitine inhibited the mRNA expression of BCL2 anti-apoptotic gene and increased the expression of BAX, TP53, CASP9 and CASP3 genes. Our results from this experiment are convergent with other studies on coumarin derivatives. Finally, it should be noted that grandivitine can be an effective substance in the treatment of cancer.

Keywords: Lung cancer, apoptosis, A549, Grandivittin

3-year study of surgical wound infection in a gynecological and pediatric Educational and Medical Center in Semnan. (Research Paper)

Faezeh Valian,[1] Seyedeh Fatemeh Nabavi Chashmi ,[2] Samaneh Chenari ,[3] Fereshteh Ghods ,[4] Mohadeseh Saffari ,[5,*]

1. Master student of intensive care nursing, Semnan University of Medical Sciences, Semnan, Iran.
2. Nurse of Infection Control Committee of Amir Al-Momenin Educational and Medical Center, Semnan University of Medical Sciences, Semnan, Iran.
3. Student Research Committee, School of Allied Medical Sciences, Semnan University of Medical Sciences, Semnan, Iran.
4. Head Nurse of Amir Al-Momenin Educational and Medical Center, Semnan University of Medical Sciences, Semnan, Iran.
5. Faculty member of School of Allied Medical Sciences, Semnan University of Medical Sciences, Semnan, Iran.

Introduction: Surgical wound infection is the second most common cause of nosocomial infections, accounting for at least 17% of these cases. Infection of the surgical wound site has irreversible complications, so that it is one of the causes of mortality due to surgery and the additional costs caused by it, result in a long stay in the hospital. Lack of knowledge about its prevalence can impede preventive decisions in the general policies of the health system. Therefore, the present study was performed with the aim of 3-year study of surgical wound infection in a gynecological and pediatric Educational and Medical Center in Semnan.

Methods: This descriptive cross-sectional study was performed from 1396 to 1399 in Amir Al-Momenin Hospital in Semnan. After referring to all the data in the hospital infection control committee, the necessary information was collected and then analyzed by SPSS software version 23 with the help of descriptive statistical methods.

Results: The results showed that the prevalence of surgical wound infection based on the total number of surgeries performed in this center in 1399, 1398 and 1397 was 0.4, 0.8 and 0.7%, respectively. The results also showed that according to the type of hospital ward, the highest rate of infection during these three years were related to gynecological surgery wards 85.8% (38 cases), vip (including gynecological surgery and other surgeries in female patients) 11.3% (5 cases) and pediatric surgery ward was 2.2% (1 case). The results showed that the highest rates of infection were related to cesarean section, hysterectomy and laparotomy, respectively. Out of 44 patients with surgical wound infection, 34 (77.2%) had superficial infection and 10 (22.7%) had deep infection.

Conclusion: Based on the results of this study, it is recommended that health issues, aseptic principles and more effective preventive strategies be considered to reduce the incidence of surgical wound infections in hospitals and surgical centers. Permanent monitoring with mechanisms planned by the Infection Control Committee of hospitals and also further researches in identifying susceptible cases of surgical wound infection are also recommended.

Keywords: Nosocomial infection, Surgical wound infection, Surgery.

A Brief Review on Dermal Fillers (Review)

Ariga Nazarian,[1,*] Atefeh Solouk Mofrad,[2] Masoud Hafezi Ardakani,[3] Masoumeh Haghbin Nazarpak,[4] Ali Rastgoftar,[5]

1. Biomedical Engineering Department, Amirkabir University of Technology (Tehran Polytechnic), Tehran, Iran.
2. Biomedical Engineering Department, Amirkabir University of Technology (Tehran Polytechnic), Tehran, Iran.
3. Biomedical Engineering Department, Amirkabir University of Technology (Tehran Polytechnic), Tehran, Iran.
4. New Technologies Research Center (NTRC), Amirkabir University of Technology, Tehran, Iran.
5. Biomedical Engineering Department, Amirkabir University of Technology (Tehran Polytechnic), Tehran, Iran.

Introduction: Due to the importance of grace throughout history many techniques have been designed in order to rejuvenate and treat dermal defects. The use of soft tissue fillers has become an essential tool in aesthetic rejuvenation. The ideal dermal filler should be safe, inexpensive, hypoallergenic, easy to store, painless to inject, require no allergy testing and have no risk of complications. Skin fillers today are categorized into biodegradable or resorbable, and permanent or non-resorbable fillers. Resorbable fillers divided into two categories: (1) nonpermanent fillers also known as replacement fillers such as fillers based on collagen, hyaluronic acid, which have short durability and are resorbed through macrophage activation: (2) semipermanent fillers or stimulatory fillers such as polylactic acid (PLLA) and calcium hydroxyapatite (CaHA) based dermal fillers, which have longer lasting results, they cause foreign body reactions that motivate fibroblast activation and collagenesis at the site of injection. Permanent fillers/implants like polymethylmethacrylate (PMMA) and silicone could provide long lasting results, but with high risk of complications. In this article we discuss the most common types of fillers, their characteristics and complications.

Methods: In this study, we have been used the method of library collection, search in various texts and authoritative scientific articles and 54 articles about dermal fillers and their characteristics from PubMed and Google Scholar have been reviewed.

Results: Facial tissue aging and volume loss have been treated for more than a century, as fat grafting reported as early as 1893. In the early 1900's liquid paraffin had been utilized for facial rejuvenation but regarding the high rate of complications stopped soon. In the 1970's and 1980's, silicone gel had been utilized, that consists of solid silicone particles suspended in a polyvinyl

pyrrolidone carrier. According to many complications like chronic inflammation and granuloma formation had been transferred by means of PMMA suspended in a bovine collagen. Owing to non-biodegradability of PMMA, this filler is permanent, therefore utilization of this kind of filler had not been noticed very well. A skin test is necessary before treatment to determine possible sensitivity to bovine collagen as it may cause hypersensitivity reactions. The main concern about the use of permanent filler, is the possibility of late-onset adverse events or displacement of the material when facial structures change with the aging process. The first filler which was approved by FDA to correct the signs of facial fat loss, was poly-L-lactic acid (PLLA) in 2004. PLLA is considered to be a deep tissue regenerator, providing soft tissue augmentation through stimulation of fibroblast production. Injectable gels based on Hyaluronic acid (HA) are the other non-permanent type of dermal fillers which does not need allergy testing and has better durability toward early fillers. Many factors are effective on ultimate properties and injectability of gel, hence the accessibility of ideal fillers based on HA won't be convenient so much. Due to many complications caused by early fillers, these days composite fillers, like fillers based on Calcium hydroxyapatite has been noticed due to traits like non pyrogenic, biocompatibility, biodegradability, non-migratory, and appropriate durability (12 to 18 months). Although these fillers don't cause antigenic effects and have capability of sterilization. The best aesthetic results are achieved when selecting the appropriate filler. The appropriate filler should be selected based on site of injection, patient-specific goals and tissue properties.

Conclusion: In this study, we tried to give a brief and useful study of dermal fillers material and properties. As we noticed in article, there are number of dermal fillers which are used for treatment but composite dermal fillers are novel rejuvenate candidates, and have potential to treating facial aging symptoms with least number of side effects as compared to other dermal fillers. Incorporation of primary gels with other materials like hydroxyapatite achieve the desired results for ideal filler, such as safety, non-immunogenicity, minimizing any risk of an allergic reactions, non-migratory and etc. Continued innovations in facial fillers are aimed at developing longer-lasting and more natural products with fewer adverse effects and improved patient-reported outcomes.

Keywords: Soft tissue fillers, Calcium hydroxyapatite, Dermal fillers, Rejuvenation, Injectable fillers

A Comparative Study on the Effects of Nephrotoxicity in Teicoplanin and Linezolid Injection in Patients with Vancomycin-Resistant Gram-positive Infections Admitted to Selected Education Centers of Alborz University of Medical Sciences in 1396 (Research Paper)

sara khodayar,[1] iraj javadi,[2,*] mahdi azimian zavareh,[3]

1. Department of Toxicology, college of Pharmacy , Shahreza branch, Islamic Azad University, Shahreza, Iran
2. Department of Toxicology, college of Pharmacy , Shahreza branch, Islamic Azad University, Shahreza, Iran
3. Department of Developmental Biology, college of Basic Sciences , Science and Research branch, Islamic Azad University, Tehran, Iran

Introduction: Teicoplanin and Linezolid have an impact on the spectrum of gram-positive bacteria resistant to vancomycin. According to previous studies, there are conflicting reports of the effects of these two drugs on the hepatorenal and thrombocytopenic systems, The aim of this study was to evaluate the effects of nephrotoxicity in Teicoplanin and linezolid injection in patients with vancocomycin resistant gram positive infections in selected educational centers of Alborz University of Medical Sciences in 1396.

Methods: Randomized sampling was performed from patients hospitalized in different hospitals of Alborz University of Medical Sciences (Shahid Madani, Shahid Rajai, Shahid Bahonar, Kamali) with vanocomycin-resistant gram-positive bacterial infections. Samples were taken 10 consecutive days and measure renal markers such as urea, creatinine, glucose filtration rate (GFR). On the other hand, two important markers of kidney damage of albumin and Kim-1 were also evaluated by Kite Eliza for confirmation of renal markers. 123 patients were divided into six groups based on the use of linezolide or Teicoplanin and the age group (three age ranges: 18-29 years old, ages 30-49, and more than 50 years old). The control group was also considered in all three age groups including healthy people who did not receive any medication.

Results: The data of the study showed that The data of the study showed that Teicoplanin and linezolid in people over 50 years of age had an effect on GFR, thrombocytopenia and urea levels, and these effects were less pronounced in the age group of 30-49 years. On the other hand, in two age groups of 30 to 49 years and more than 50 years, after ten days of using these antibiotics, both drugs have a significant effect on the amount of two kidney damage biomarkers of albumin and Kim-1. Teicoplanin and linezolid in people over 50 years of age had an effect on GFR and these effects were less pronounced in the age group of 30-49 years. On the other hand, in two age groups of 30 to 49 years and more than 50 years, after ten days of using

these antibiotics, both drugs have a significant effect on the amount of two kidney damage biomarkers of albumin and Kim-1.

Conclusion: The results of this study indicate the prognosis of kidney damage in long-term administration of drugs and should be given more precisely at the clinic according to the age category of subjects and the field of kidney disease, dosage and duration of use of these antibiotics.

Keywords: Ticoplanin, Linzolide, Nephrotoxicity, Albumin, Kim-1, vancomycin

A comparison of prevalence Human herpes virus 6 (HHV-6) between patients with Hashimoto's thyroiditis and healthy individuals through polymerase chain reaction method (PCR) in thyroid biopsy specimen (Research Paper)

Zahra Darvish molla,[1,*]

1. Islamic Azad University, Tehran Medical Sciences & technology

Introduction: Hashimoto's thyroiditis is a chronic inflammation of the thyroid gland and an autoimmune disease that causes hypothyroidism. Genetic, internal and environmental factors are the causes of this disease. Due to the fact that human herpes viruses such as herpes virus type 6 (HHV-6) are involved in some autoimmune disorders, they may also play a role in causing this disease.

Methods: In the present study, 64 samples of thyroid paraffin tissue (32 samples of thyroid paraffin tissue of healthy individuals as control and 32 samples of thyroid paraffin tissue of Hashimoto's thyroiditis patients) were taken from the pathology department of Loghman Hakim Hospital in Tehran. Demographic information of patients was collected by a questionnaire. After DNA extraction from the samples, Nested PCR technique was performed using specific primers and the reaction product was electrophoresed.

Results: Herpes virus type 6 genome results in thyroid tissue of 34.4% of healthy individuals (81.8% female and 18.2% male) and 46.9% of patients with Hashimoto's thyroiditis (73.3% female and 26.7% male). It was found that this difference in virus frequency between the two groups was not statistically significant (P value=0.309). There was also no statistically significant relationship between the prevalence of human herpes virus type 6 and age and sex.

Conclusion: Comparison of HHV-6 infection between control and patient groups showed that although the number of infected people in Hashimoto's patients was higher than the control group, but this difference was not statistically significant; Therefore, HHV-6 can not be associated with Hashimoto's thyroiditis.

Keywords: Hashimoto's thyroiditis, Autoimmune disease, Human herpes virus type 6, Polymerase chain reaction.

A comparison of the effectiveness of current treatment methods of echinococcosis (Review)

Amir Ardalan Shokrollahi,[1,*] pollet betbenyamin,[2]

1. Rab-e-rashid Higher education institute
2. Rab-e-rashid Higher education institute

Introduction: Although humans are accidental hosts for Echinococcoccus tapeworms, echinococcosis possesses serious threats for rural populations and requires precise microbiological prevention actions. Echinococcosis has two major infectious species. One of them being E.granulosis and E.multilocularis, which have the same definitive host while differentiating in intermediate hosts. Dogs, wolves, and foxes are the definitive host for both species, while E.granulosis utilizes sheep and cattle the latter uses rats as their intermediate host. Diagnosing the infected animal and following a quick and effective treatment is the most efficient action plan to prevent more infections whilst keeping the economic losses to the minimum. As such identifying, the most effective treatment method is very important. Since the discovery of Benzimidazoles, Mebendazole and Albendazole are two of the most efficient drugs to treat echinococcosis at the larval stage. Researchers found that Albendazole is the most efficient drug in the early stages of the disease development. Another invasive way to inhibit cystic echinocccosis specifically is to use the PAIR method (Puncture, aspiration, injection of a scolecidal agent, and reaspiration.) which involves the injection of a scolicidal agent that aims to destroy the germinal membrane. Although this method holds a massive therapeutic advantage but comes with certain blocks, such as limitation of the operating area, cysts that have high solid material, and cyst that bears multiple daughter vesicles. Also, it is not recommended to utilize PAIR method for cysts that contain materials that cannot be absorbed, also cyst in critical areas that have the risk of spreading into the abdominal cavity, peritoneal cavity or biliary tract renders PAIR method ineffective. Surgical treatment is the most common invasive method up to this day, and currently, it is only applied to the complicated cysts that may have developed perforated cysts or biliary fistula. Surgical treatment is also applied to the cysts that bear daughter cysts. Considering the amount of invasion in surgical operations this paper focuses on the comparison of non-invasive or partially invasive methods in the treatment process of chinococcosis.

Methods: In this review, online scientific databases such as The National Center for Biotechnology Information and Google scholar have been used. This article is a result of more than 35 articles of which 14 of them have been used directly.

Results: Comparing the effectiveness of various treatment methods and identifying the most efficient treatment is severely important. However, cyst size and classification is a differentiative factor in treatment path. In general cysts smaller than 5 cm are treated with albendazole, providing effectiveness in the early infection phase, while larger cysts require the PAIR method and Albendazole treatment to control the cyst, however in both AE and CE cases, radical surgeries have been proven to be more effective.

Conclusion: Iran has been identified as an endemic country for Hydatid disease and has an average higher than some of the countries. Livestock slaughtering outside the certified facilities and lack of veterinary supervision might be of an amplifying element. A novel treatment method is required so that echinococcosis could be dealt with efficiently. Also, more comparative research is required to provide the time sensitivity of this disease.

Keywords: Human cystic echinococcosis, hydatid disease, parasiticide, zoonosis

A new strategy in improving therapeutic indexes of medicinal herbs: characterization of nano-liposomes containing Mentha piperita essential oil (Research Paper)

Maryam Cheshmberah,[1] Mohammad Javad Forouzani-Moghaddam,[2,*]

1. MSc of Genetic, Sistan & Balochestan university, Zahedan, Iran
2. Msc of Food Microbiology, School of Paramedical, Iran University of Medical Sciences, Tehran, Iran

Introduction: Herbal Compound and their essential oils possess high antimicrobial, antioxidant, and anti tumor properties, but conventional prescribing of them faces serious challenges. Liposomal nano carrier is one of the common pharmaceutical strategies to overcome these challenges. In this study, slow released liposomal system containing Mentha piperita's essential oil was prepared in order to improve its antimicrobial, antioxidant and antitumor properties.

Methods: Liposomal vesicles were prepared using phosphatidylcholine (80%) and cholesterol (20%) by thin film method. Mentha piperita's essential oil were loaded into the liposomes using inactive loading method. Their physico chemical features were assayed using Zeta Sizer, FTIR and at the end, the essential oil release amount was calculated at 37° C.

Results: Liposomal vesicles containing Mentha piperita's essential oil showed the size of 247 nm, 61.38% essential oil encapsulation efficiency, -34.54 mV of zeta potential and polydispersity index (PDI) of 0.32. The prepared liposomal system presented essential oil controlled release and FTIR investigation showed no interaction between nanocarrier and the essential oil and the carriers have spherical structures.

Conclusion: In the present study, Mentha piperita's essential oil encapsulated in liposomal carriers and its physicochemical properties investigated. The results confrimed the slow releasing ability of system and also showed that the anionic nanosystem increased the essential oil's stability without any change in its chemical nature. Taken together, liposomal nanocarrier could be a potent and suitable carrier for the essential oil.

Keywords: Liposome, therapeutic herbs, Mentha piperita, Plant Oils

A novel low cost non-enzymatic glucose sensor based on nanoporous cobalt sulfide nanosheet arrays (Review)

Aida Mofazzal Jahromi,[1,*] Rahil Mosallanejad,[2] Seyyed Ebrahim Moosavifard,[3] Ali Rayatinejad,[4] Farnaz Abbasi,[5]

1. Student research committee, Jahrom University of Medical Sciences, Jahrom, Iran
2. Student research committee, Jahrom University of Medical Sciences, Jahrom, Iran
3. Zoonoses Research Center, Jahrom University of Medical Sciences, Jahrom, Iran
4. Student research committee, Jahrom University of Medical Sciences, Jahrom, Iran
5. Student research committee, Jahrom University of Medical Sciences, Jahrom, Iran

Introduction: Diabetes mellitus is the ninth leading cause of death globally, which is expected to reach 366 million patients by the year 2030. Due to the risks of diabetes-induced diseases and high healthcare expenditures, which are mainly caused by lack of continuous glycemic control, finding techniques for frequent monitoring of blood glucose has become one of the main concerns of modern society. Among methods of blood glucose evaluation, electrochemical sensors are so promising for optimal therapeutic interventions as well as improving the quality of diabetic patients due to their simplicity, low cost, high accuracy, and speed. Moreover, researchers are getting more interested in developing none enzymatic sensors by reason their disposability, rigidity, stability, high sensitivity, simple synthesis process, and ability to combine them with different nanomaterials.

Methods: In this research, the nanosheets of cobalt sulfide were electrochemically (using the chronoamperometry technique at a potential of -1.2 V relative to the silver/silver chloride reference electrodedeposited on the surface of pencil graphite and used directly as a non-adhesive non-enzymatic electrode to measure glucose in a 3-electrode system. The electrocatalytic efficiency of this electrode for the oxidation of glucose in 0.1 molar sodium hydroxide electrolyte (pH=13) and in the potential of +0.55 V was evaluated using cyclic voltammetry and amperometry techniques. Also, the structure and morphology of the as-prepared electrode were investigated by X-ray diffraction (XRD) and scanning electron microscope (SEM).

Results: Electrochemical studies showed that this electrode has a linear amplitude in the range of 2 to 5000 µM, detection limit of 0.3 µM, and sensitivity of 1985 µA/mM cm2. Also, the study of the electrode responses during 3 months for a concentration of 2 mM glucose showed stability of

90.4%, which indicates high stability of this electrode. Finally, the amperometric responses of this electrode in human serum samples were compared with the commercial glucometer responses

Conclusion: A low glucose detection limit of 0.3 µM, long-term stability, wide linear amplitude, and high sensitivity, highlight the promising performance of the cobalt sulfide nanosheets on pencil graphite electrode for cost-effective non-enzymatic glucose sensing with high favorable reproducibility.

Keywords: Non-enzymatic sensors, cobalt sulphide, glucose, pencil graphite

A novel method for biosensor fabrication based on target recycling and polymerization signal amplification strategies (Review)

Aria Raoufi,[1,*]

1. Dr. Mohammad Shafiee's High School

Introduction: The detection of microRNAs (miRs) with the specific sequence is an important factor in the disease's diagnosis. In this study, a double signal amplification electrochemical biosensor for sensitive detection of miRNA-21 based on a duplex-specific nuclease (DSN)-assisted target recycling was developed which combined with electrochemically mediated surface-initiated ATRP (eATRP) signal amplification.

Methods: In the absence of target miRNA, hairpin DNAs (hDNAs) provide a high density of phosphate groups for the subsequent attachment of eATRP initiators onto the electrode surface utilizing the phosphate-Zr4+-carboxylate chemistry, followed by the de novo growth of electroactive polymer via the SI-eATRP. De novo growth of long polymeric chains enables the labeling of numerous electroactive probes, which produce a highly electrochemical response.

Results: In the presence of target miRNA, the hDNA on the electrode surface hybridizes with target miRNA (T-miR) and forms RNA/DNA duplexes, which become the substrate of the DSN. As DSN cleaves only the DNA strands in the duplexes, the target miRNA is released and then hybridized with another hDNA.

Conclusion: Finally, in this "signal off" method, the electrochemical signal reduced in the presence of T-miR because of the elimination of a large amount of hDNA by one miRNA. Furthermore, this method can distinguish similar miRNAs that differ by only one base due to the strong differentiating ability of DSN. Ultimately, the proposed biosensor has great potential to provide a platform for the sensitive and selective detection of miRNAs.

Keywords: Electrochemical biosensor, MicroRNAs, Duplex specific nuclease

A novel tethering approach using monomeric streptavidin improves CRISPR-Cas9 genome editing efficiency in CHO cells (Research Paper)

Mohammad Hassan Kheirandish,[1] Behnaz Rahmani,[2] Mohammad Ali Mazlomi,[3] Hossein Zarei Jaliani,[4] Fatemeh Davami,[5,*]

1. Department of Medical Biotechnology, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran
2. Medical Biotechnology Department, Semnan University of Medical Sciences, Semnan, Iran
3. Department of Medical Biotechnology, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran
4. Department of Medical Biotechnology, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
5. Biotechnology Research Center, Pasteur Institute of Iran, Tehran, Iran

Introduction: CRISPR-Cas9 is becoming a leading tool to introduce defined changes into the pre-determined site of the genome by Cas9-mediated double strand break (DSB). Once the break is generated, knock-in can be occurred by homology-directed repair (HDR) mechanism when a repair template is provided at the DSB site. However, the low rate of HDR remains a key challenge in efficient knock-in at the most types of the cell. Recently has been found that tethering of donor template and Cas9 endonuclease and co-localizing them to the nucleus, improve the efficiency of knock-in via CRISPR-Cas9. In this regard, our study aimed to design a novel construct with the monomeric form of streptavidin that was genetically fused to the C-terminus of Cas9 protein and co-transfect it with the biotinylated donor to the Chinese hamster cell line.

Methods: Monomeric streptavidin (mSA) gene was amplified by polymerase chain reaction with primers complementary to the all-in-one (Cas9/sgRNA) vector backbone and mSA gene. First PCR using these primers was conducted to synthesize chimeric Cas9-NLS-mSA fragment. The product of the first PCR was gel purified and used as a mega primer in a quick-change PCR to synthesize the remaining parts of the all-in-one vector. The product was digested with DpnI restriction enzyme. Simultaneously we benefited from biotinylated primers to create biotinylated donor harboring GFP reporter and puromycin selection marker sequences flanked by long homology arms. Both constructs were transfected to CHO-K1 cell line using lipofectamine 3000 reagent. (Cells in the control group transfected by the circular donor and Cas9/sgRNA vector). Transfection efficiency has been evaluated by fluorescent microscopy and Flow cytometry for GFP expression. 72 hours after transfection, stable cell lines have been generated using 3.5 µg/mL of puromycin in the 6-well plate for 14 days. Cell pools of both groups were analyzed by 5'/3' junction PCR. Clonal selection has been done in 96-well.

After 7 days each well including single-cell colonies that expressed GFP reporter were trypsinated and transferred to the 24-well. After genomic DNA extraction 5'/3' junction and out-out PCR analysis have been performed for each recovered clone to estimate overall knock-in efficiency.

Results: Monomeric streptavidin sequence with a suitable linker was fused to the 3' end of the Cas9 gene and cloned into the all-in-one vector by the restriction endonuclease free cloning method. The inserted sequences were confirmed by DNA sequencing. Cas9-mSA/sgRNA vector and biotinylated donor have been transfected to the CHO-K1 cell line and transfected cells were observed by fluorescent microscopy. Stable cell lines have been created after two weeks of the antibiotic selection procedure. 5'/3' junction PCR analysis on the cell pool showed desired bonds on 1% gel agarose electrophoresis. After limiting dilution, 39 single clones have been recovered for the tethering group and 49 clones for the control group. Each individual clones ubiquitously expressed GFP reporter, among which 20 clones of tethering and 10 clones of control groups were 5'/3' junction PCR positive. Further analysis showed that 15 of 39 and 6 of 49 clones were out-out PCR positive for tethering and control groups respectively.

Conclusion: In this study, we enhanced the targeted efficiency of knock-in via CRISPR-Cas9 in the CHO-K1 cell line as a leading host for biopharmaceutical production. With a tethering approach using a novel construct of Cas9-mSA/sgRNA and easy to create PCR amplified biotinylated donor, we achieved more than 3 fold enhancement of knock-in efficiency in CHO-K1 cells compared to the conventional CRISPR-Cas9 to insert the large transgene cassette (~2 kb). This approach could propose a simple and efficient strategy for enhancing targeted knock-in efficiency in the Chinese hamster cell line.

Keywords: CRISPR-Cas9, tethering approach, Monomeric streptavidin, CHO-K1

A Pathological and structural Study of Cardiac, Forceps Striated Muscles, microscopic Changes of Liver and kidney following Short Term Resistance Training in male Rats (Research Paper)

Saber Ghaderpour,[1] Rafighe Ghiasi,[2,*]

1. Department of Physiology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
2. Department of Physiology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

Introduction: Resistance exercise, known as stretching and weight training, is a special method designed to increase traction and muscle endurance. In response to this type of exercise, skeletal and cardiac muscle adapt and beneficial physiological changes occur in other tissues. This study was conducted to evaluate the effects of Short Term Resistance Training on Pathological and Ultrastructural changes of Cardiac, Forceps Striated Muscles, microscopic Changes of Liver and kidney.

Methods: Twenty adult male Wistar rats were randomly divided into control and exercise groups. The exercise group performed Short Term Resistance Training for one month. At the end of the course, the animals were first anesthetized and then autopsied and isolated tissues such as heart muscle, Forceps muscle of the right leg, liver, and kidney are performed and the isolated tissues are stabilized in 10% neutral buffer in formalin solution. After tissue preparation and preparation of paraffin blocks, sections with a thickness of 5 microns are prepared and transferred to the slide and after staining by hematoxylin-eosin (H&E) method are studied by light microscopy.

Results: Histopathological changes in liver tissue in the control group included mild hyperemia. The liver also showed mild degrees of reactivity, with an increase in the size and number of kupffer cells. The infiltration and settlement of neutrophils were visible in the disse space. The liver tissue in the exercise group showed mild hyperemia, the severity of hyperemia was slightly higher than the control group. In exercise group, the liver also showed mild degrees of reactivity, with an increase in the size and number of Kupffer cells. Also, the infiltration and settlement of neutrophils in the disse space was visible. Sinusoid dilation and mild fat change were also observed. In the control group, no complications were seen in cardiac tissue except hyperemia. In the cardiac tissue of the exercise group, mild hyperemia, mild degeneration of the cardiac muscle cells, mild lesions with a transverse cross-section of the muscle cells, and greater staining and hyaline of these cells were seen. Compared with the control group, muscle cell hypertrophy was observed in this group. The Forceps muscle tissue in the control group showed hyperemia. The Forceps muscle tissue of the exercise group showed

mild hyperemia, mild damage lesions with loss of transverse muscle cell translocation, and greater staining and hyaline depletion of these cells. Compared with the control group, muscle cell hypertrophy was observed in this group. In the renal tissue of the control group, no complication was observed except mild hyperemia. Also, no complications other than mild hyperemia were seen in the exercise group.

Conclusion: In general, short-term exercise in male rats had positive effects on body tissues.

Keywords: Short-term exercise, Cardiac tissue, liver tissue, Forceps Striated Muscle, kidney tissue.

A review of colorectal cancer (Review)

Shokripour ramin,[1,*] Ranjbar ramesh,[2]

1. 1. Department of Biotechnology, faculty of Biological Sciencen and Technology, Shahid Ashrafi Esfahani University, Isfahan, Iran
2. 1. Department of Biotechnology, faculty of Biological Sciencen and Technology, Shahid Ashrafi Esfahani University, Isfahan, Iran

Introduction: Colorectal cancer is the second deadliest cancer and the third most common cancer in the world after prostate cancer in men, breast cancer in women and lung cancer, which is more common in men than women. Colorectal cancer is one of the few cancers that screening, early diagnosis and timely treatment can significantly control it. Therefore, familiarity with this cancer, identifying the causative agents, diagnosis, treatment, etc. is very important. This article addresses this issue.

Methods: This research is a review study and, in this research, Iranian and foreign databases such as PUBMED, NCBI, etc. have been used to collect information.

Results: According to the findings, the increase in colorectal cancer is increasing in developed countries, and this is due to the growing population, modern unfavorable eating habits and increasing risk factors such as smoking, low physical activity and obesity.

Conclusion: According to studies and documents, environmental and genetic factors play a major role in the pathogenesis of colon cancer. The role of nutrition in colon cancer has also been studied and the results indicate that it is an effective factor in creating or protecting against this cancer. Also, the mortality rate from colon cancer has decreased due to effective cancer screening measures, so it is important to observe environmental factors such as nutrition in prevention and screening to reduce mortality from this cancer.

Keywords: cancer, Cancer prevalence, Epidemiological Studies.

A review of Epigenetic in cancer (Review)

Maliheh Hosseinpour,[1,*]

1.

Introduction: Epigenetics is defined as an inherited change in gene expression or chromosomal stability. Epigenetics, along with genetic mechanisms, is essential for the natural evolution and maintenance of gene expression patterns in mammals. Waddington Conrad introduced the term epigenetics in 1942s. Epigenetic changes can be caused by factors such as environmental factors, diet, medications, and smoking. Cancer is a disease caused by molecular changes with genetic or epigenetic origins. Activation of oncogenes or inactivation of tumor suppressor genes (TSG's) by mutations are among the major genetic changes involved in cancer. Epigenetic changes regulate hereditary changes in the development of human cancers. In epigenetic changes, abnormal patterns of DNA methylation, patterns of histone post-translational changes, and changes in chromatin composition and organization can be observed. This review discusses the concept of epigenetic changes in cancer and the use of this knowledge in the design of new treatments.

Methods: This study has performed by searching the "PubMed database" and "Google scholar" by different combinations of terms "epigenetic" and "cancer". DNA methylation, histone modifications, nutrition, and their effects on cancer cells investigated.

Results: Epigenetic changes, unlike genetic changes, are dynamic and reversible. The reversible nature of epigenetic changes has led to the emergence of new epigenetic therapies. For example, different types of drugs have been developed that target DNA methyltransferases. The idea of using these drugs is to block the enzymes that control DNA methylation in cancer. On the other hand, in many cases, a range of foods may contain biologically active compounds that are effective in preventing cancer, and may also facilitate epigenetic changes. Therefore, food intake may help prevent cancer.

Conclusion: Due to the presence of several epigenetic disorders in many diseases, changes in the epigenome can be used to predict the risks of cancer, and epigenetic therapy seems to be a successful method for treating various malignancies.

Keywords: Cancer; DNA methylation; Epigenetics; Histone modifications; Nutrition.

A review of intervention affecting the quality of life of women with polycystic ovary syndrome (Review)

Mahbobe omid,[1,*] Zhila ganji,[2]

1. Nasibeh nursing and midwifery faculty Mazandaran University of Medical science
2. Nasibeh nursing and midwifery faculty Mazandaran University science

Introduction: Introduction & Objective: Polycystic ovary syndrome is the most common endocrine disorder between the women of reproductive age which is diagnosed with symptoms such as hyperandrogenism, oligomenorrhea or amenorrhea and cystic appearance of the ovary. Based on the results of various studies, the prevalence of polycystic ovary syndrome has been reported to be 2.26-26%. Studies that have examined the quality of life in patients with this syndrome have shown that biochemical, hormonal, metabolic factors and also physical issues such as infertility and menstrual irregularities have a negative impact on the quality of life and mental health of these patients. Numerous studies have been conducted to improve the quality of life of these women around the world and the present study has been done with the target of review the interventions affecting in the quality of life of the women with poly cystic ovary syndrome.

Methods: Methods: The present study is a review study written by researchers with keywords such as polycystic ovary syndrome, quality of life, interventions, women of childbearing age and their English equivalent polycystic ovarian syndrome (PCOS), quality of life, interventions and reproductive aged women searched databases such as Google Scholar, Magiran, Irandoc, SID, PubMed and Web of Science and extracted studies related to the title of the present study. Inclusion criteria were high quality clinical trial studies and studies examining the quality of life in women with polycystic ovary syndrome.studies published in non-Persian and English languages and studies that have referred to surgical interventions are excluded from the present review study.Initially, 366 studies were searched and after screening the title, abstract and full text of the articles, finally 16 articles that were published during the years 2020-2005 were used to compile the present study.

Results: Results: The results of the present study were presented on interventions affecting the quality of life of women with polycystic ovary syndrome in four categories. The first category of drug interventions affecting the quality of life of women with PCOS (treatment with metformin and OCP includes 5 articles), the second category of lifestyle interventions on the quality of life of women with PCOS (exercise such as continuous and intermittent aerobic exercise interventions, diet and change Lifestyle to reduce

anthropometric indices and hyperandrogenism (including 5 articles), the third category of complementary medicine on the quality of life of women with PCOS (acupuncture and physical activity interventions to improve depression and anxiety symptoms and poor health-related quality of life, including 2 articles) And the fourth category of psychological interventions on the quality of life of women with PCOS (cognitive-behavioral therapy for stress management and cognitive therapy includes 4 articles).

Conclusion: Conclusion: Considering that several interventions have been performed to improve the quality of life in women with polycystic ovary syndrome, which in many cases their effectiveness has been confirmed in the study of population, Therefore considering the best therapeutic interventions mentioned according to the patient's condition based on the treatment team is important and necessary.

Keywords: Keywords: Polycystic Ovary Syndrome, Quality of Life, Interventions, Women of childbearing age

A review of Mediterranean spotted fever in Iran (Review)

Reza Khoshbakht,[1,*] Fatemeh Moammeri,[2]

1. Department of Laboratory Sciences, Faculty of Paramedical, Mashhad University of Medical Sciences, Mashhad, Iran
2. Department of Laboratory Sciences, Faculty of Paramedical, Mashhad University of Medical Sciences, Mashhad, Iran

Introduction: Introduction: Rickettsioses are zoonoses that are caused by bacteria (genus Rickettsia) and transmitted by arthropods all over the world. These zoonoses have been recognized across the world as emerging vector-borne infections. Human rickettsioses have become more common in recent decades. The rickettsial pathogen Rickettsia conorii causes Mediterranean spotted fever (MSF), which is spread by ticks. MSF is marked by rash, fever, and eschar at the tick bite site. Although this condition has been recognized for a long time, it has received little attention in Iran. Little research on the incidence and clinical manifestations of MSF in Iran has been done.

Methods: Method: Several search keywords were used to find all relevant publications on MSF in Iran (e.g. Rickettsioses in Iran, Tick-borne rickettsioses in Iran, Mediterranean spotted fever in Iran, Rickettsia conorii in Iran). The search was limited to authentic materials from prominent database repositories among them PubMed, Web of Science, Google Scholar, Science Direct, SCOPUS, and SID by two persons individually. The search items included peer-reviewed journals, books, and book chapters published between 1996 and 2021.

Results: Result: A total of 43 scientific articles and reports were found, with 13 of them meeting the search criteria and being reviewed. Two of the 13 studies studied MSF in Iran, while the other eleven investigated vectors potentially spread Rickettsia conorii to humans. Serological methods used on samples taken from patients revealed the presence of Rickettsia conorii.

Conclusion: Discussion: In past years, rickettsial infection in Iran may have been underreported. Misdiagnosis is due to a variety of factors, including a lack of expertise and inadequate diagnostic methods. Several countries have a large number of ticks that can spread rickettsiae (e.g. Yemen, Saudi Arabia, Turkey, and Oman). Because all of these factors are present in the Middle East, the disease is extremely likely to spread in the region. Despite strong evidence of organisms that cause MSF in the Middle East, few investigations on the disease have been done in Iran. As a result, investigations on MSF Rickettsiae are needed to better understand the epidemiology in Iran.

Keywords: Keywords: Mediterranean Spotted Fever, Rickettsia conorii Infection, Rickettsioses, Tick, Iran

A review of Neisseria meningitidis in Iran (Review)

Maryam Rad,[1] Gholamhossein Ebrahimipour,[2] Mojgan Bandehpour,[3,*] Omid Akhavan,[4] Fatemeh Yarian,[5]

1. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
2. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
3. Cellular and Molecular Biology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran-Department of Medical Biotechnology, School of Advanced Technologies in Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
4. Department of Physics, Sharif University of Technology, Tehran, Iran
5. Cellular and Molecular Biology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran-Department of Medical Biotechnology, School of Advanced Technologies in Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Introduction: Meningitis, which is mostly caused by bacteria, fungi and viruses, and in some cases is caused by chemical irritation, subarachnoid hemorrhage, cancer, etc., is defined as meningitis [1]. Bacterial meningitis, especially meningitis caused by Neisseria meningitidis, is one of the most dangerous infectious diseases [2]. According to the World Health Organization, between 300,000 and 350,000 people get meningococcal disease each year [3]. In this article, we will review meningococcal meningitis in Iran. Neisseria meningitides: Neisseria meningitides is a gram-negative bacterium. It is hosted by humans. This bacterium has 13 serogroups (A, B, C, D, H, I, K, L, X, Y, Z, W-135 and E-129) based on polysaccharide capsules. In different parts of the world, these strains have different distribution [4]. Invasion of Neisseria meningitides: Neisseria meningitides causes infectious diseases worldwide. Meningococcus is a major cause of bacterial meningitis and accounts for 80 to 95% of epidemics of this disease at different ages in most communities. The prevalence of meningococcal meningitis in different parts of the world is about 1 to 12 cases per 100,000 people, which increases in epidemics. Mortality from meningococcal meningitis is about 9% to 40% and the rate of stable neurological complications in survivors is about 19%. Early diagnosis and appropriate treatment are effective in reducing mortality and complications from this disease [5]. Distribution of Neisseria meningitides in Iran: In Iran, there is no suitable monitoring system in the whole country to detect the causes of bacterial meningitis and studies are limited to a specific organism and region. Table 1 shows the distribution of Neisseria meningitides in different regions of Iran. According to studies, Neisseria meningitides is the third leading cause of

bacterial meningitis in Iran by PCR (Figure 1), But based on culture, it ranks fourth in 1991 to 2002 and second in 2003 to 2013. [6].

Methods: By searching for keywords in Persian and English databases such as Google Scholar, PubMed and SID related articles were selected and reviewed.

Results: Although meningitis has a low prevalence in Iran compared to other countries,if the PCR is used instead of culture, the real statistics are likely to be higher. On the other hand, part of the results is due to the antibiotics used before hospitalization [6].

Conclusion: Because meningitis is a medical emergency and its correct and timely diagnosis is important, it is expected that a unified program will be implemented to manage this disease throughout the country.

Keywords: Iran, Neisseria meningitides, Meningitis

A review of the causes of test anxiety among medical students (Review)

samaneh chenari,[1,*] mohadese saffari,[2]

1. Student Research Committee, Semnan University of Medical Sciences, Semnan, Iran
2. Faculty of paramedical school, Semnan University of Medical Sciences, Semnan, Iran

Introduction: In the present age, which is the age of academic and scientific competitions, the anxiety of exams is increasing day by day, which distracts the attention of the person and with busy thinking, information processing decreases and it can affect the academic performance and disrupt the success of the person in the exam; therefore, the causes of test anxiety among students should be investigated. The aim of this study was to investigate the causes of test anxiety among medical students.

Methods: This study was a review and information was extracted from Google Scholar, Pub med and Scopus databases by searching for the words “anxiety”, “exam”, “students”, “University of Medical Sciences”, and articles and researches on the causes of test anxiety among students of different disciplines of Medical sciences were reviewed.

Results: The majority of students had moderate or high levels of anxiety, of which the most anxiety was seen among female students. Causes of anxiety among medical students include high volume of courses, study style, lack of physical activities, duration of exams, fear of not getting enough grades, exam system, lack of time management, difficult exam questions and strict procedures established by Professors and universities. Students' anxiety was also associated with their physical, emotional and cognitive health.

Conclusion: It seems that universities should develop curricula and exam patterns according to students' problems, and professors should be aware of the factors that cause exam anxiety. It is also recommended to implement programs to prevent this anxiety and provide psychological services and counseling to identify its causes and plan to eliminate the causes.

Keywords: Examination anxiety, students, medical sciences, medical students

A review of the disadvantages of using mesenchymal stem cells (Review)

saeedh kheiripour,[1,*]

1.

Introduction: Stem cells, with their potential for regeneration and differentiation, play an essential role in various stages of tissue growth and repair. Stem cells are divided into two types based on origin: embryonic and adult . Stem cells currently used in cell therapy are mature stem cells. These cells include hematopoietic stem cells (HSC), endothelial cells (EPCs), mesenchymal stem cells (MSCs), and organ-specific stem cells . MSCs have been used extensively in studies. However, the effectiveness and shelf life of MSCs are very short . Recent studies suggest that the main stimulus observed in MSC therapeutic function is paracrine agents secreted by these cells. The supernatant of the culture medium of these cells, called the conditional medium derived from MSC-CM mesenchymal stem cells, is a rich source of paracrine factors and is studied in a wide range of repair and treatment methods .

Methods: This search was performed on Scopus, PubMed databases with the keywords mesenchymal stem cell, paracrine secretion, conditional medium in the period 2015 to 2020. Out of 31 articles, 20 articles were selected and used in this study.

Results: Secretion-based approaches using conditioned media may have significant potential advantages over living cells in terms of production, storage, transport, product shelf life, and their potential as a ready-made biological therapeutic agent .

Conclusion: Despite the multipotency and self-renewal potential of MSCs, experimental studies have shown that only a small fraction of mesenchymal stem cells are systemically incorporated into damaged tissues, indicating beneficial effects in repair and tissue regeneration is indirect and depends on the paracrine activity of MSCs. Therefore, the use of MSC-CM removes the limitations of using stem cells as a therapeutic source for tissue regeneration.

Keywords: mesenchymal stem cells , conditional medium , paracrine

A review of the effect of mountain honey on women's reproductive health (Review)

Elnaz Abedini ,[1,*]

1. ANKARA UNIVERSITY

Introduction: Health, both individually and collectively, is undoubtedly one of the most important aspects of human life and is a necessary condition for playing social roles, and all human beings can be fully active if they feel healthy and society considers them healthy. Women's health depends on complex interactions between individual biology, health behavior, and the historical, social, economic, and political context of women's lives. Although health issues and problems are important in both sexes, but it is more important to pay attention to the health of women and girls, because girls in particular have special conditions in terms of their gender and, consequently, the responsibility and role expected by society.Consumption of natural honey for eight weeks reduces the weight of overweight and obese diabetics, without having a negative effect on blood sugar.Given that traditional medicine, complementary medicine, nutrition, therapy and the use of pragmatic foods have a special place in maintaining health and prevention and treatment of diseases, and since women's health plays an important role in family and community health, this study aims to investigate The effect of honey on women's reproductive health was assessed.

Methods: This study is a review study that was conducted to investigate the effect of honey on women's reproductive health in English and Persian articles between 2005 and 2020. To access related articles, a search was conducted on the scientific databases of ISID, Medline, Pabmod, Embass, Kochran, Google Scholar, ISI, Scopus, and Medlib. This search was conducted with the keywords Honey and Reproductive Health, Pregnancy, Postpartum, Child Labor, BreastFeeding, women Health and the Persian keywords honey and women's health, reproductive health, pregnancy, childbirth, postpartum. Criteria for selecting articles were: Articles found in 2020, which are qualitative and quantitative and related to the last 15 years (since 2000), Persian and English language articles published in domestic and foreign scientific journals related to women's reproductive health. With honey, the full text of which was available, and due to the limited studies conducted in the field of women's reproductive health and honey, in this review article only the effect of honey on menstrual pain, childbirth, episiotomy, candidiasis vaginitis is discussed. Exclusion criteria were: articles in languages other than Persian and English, articles with incomplete and unrelated data and review studies, articles that had an unknown sample size, articles in which the implementation method was not well defined.Episiotomy and cesarean section wounds Honey is one of the oldest known medicines. Its use dates back to four thousand years ago

and is used in the treatment of wounds, sunburn, eye infections. Its antibacterial, tissue repair, antioxidant and anti-inflammatory effects have been identified. Research shows that topical consumption of honey is effective in healing infectious wounds, cesarean section wounds, episiotomy wounds (perineal incisions) and burns.

Results: In the search performed in the mentioned databases and according to the inclusion criteria, a total of 76 articles were obtained, of which 45 articles (2.59%) were in Persian and 31 articles (7.40%) were in English. By removing duplicate and overlapping articles in databases, in the first stage, 25 articles remained, and finally, after applying the inclusion and exclusion criteria, thirteen articles were researched.Seifi et al., In a study that examined the effect of honey vaginal gel and clotrimazole vaginal cream on the natural vaginal flora of women with candidal vaginitis, concluded that the amount of lactobacilli in the honey group increased after completing the treatment period and improving clinical symptoms. There was a significant difference before treatment

Conclusion: A review of the literature showed that honey can be effective in healing cesarean section and episiotomy . Honey is a natural disinfectant. Because honey contains antibacterial substances, it can heal wounds well. Honey, with its many properties, accelerates wound healing. The healing effect of honey wound is due to four reasons: first: antibacterial activity, second: acidity of honey: the pH of honey is between 2.3 to 4.5 and this acidity is low enough to prevent the growth of most microorganisms, third: the osmotic effect and Fourth: Contains antioxidants and hydrogen peroxide. The presence of various antioxidants in honey includes flavonoids, monofenolics, polyphenols and vitamin C. The anti-inflammatory properties of honey may be related to the antioxidant content of honey

Keywords: Honey, vitamin C, inflammatory, clinical, women's health

A review of the effect of type 2 diabetes on skeletal muscle (Review)

saeedh kheiripour,[1,*]

1.

Introduction: Diabetes mellitus (DM) is a chronic and progressive disease that is determined by increasing blood glucose levels. Type 2 diabetes (T2D) is the most common form of the disease and accounts for 85% to 95% of cases. T2D may be asymptomatic for years, but with hyperglycemia, certain symptoms such as polyphagia, polyuria, and polydipsia appear. Long-term effects of T2D include microvascular complications (retinopathy, nephropathy, neuropathy, and myopathy) and macrovascular (coronary artery disease, peripheral vascular disease, and brain disease). Insulin resistance in skeletal muscle is an important feature of T2D. But in recent years, it has become increasingly diagnosed that T2D causes skeletal muscle atrophy and muscle fiber loss. Given the increasing number of patients with T2D, the number of people with muscle loss is expected to increase dramatically in the coming decades.

Methods: The search was conducted in the Scopus and PubMed databases with the keywords type 2 diabetes, skeletal muscle.

Results: Studies have shown that the loss of leg muscle mass in type 2 diabetic patients is partly due to increased levels of interleukin-6 and tumor necrosis factor alpha. In addition, apoptotic markers such as P53, caspase-3, and Bax / Bcl2 ratio are higher in the muscles of some models of diabetic rodents than in control muscles.

Conclusion: Diabetic hyperglycemia increases cell apoptosis, inflammation, and oxidative stress in muscles; Diabetes also affects skeletal muscle by reducing myogenic activity and mitochondrial content and increasing systemic inflammation.

Keywords: Type 2 diabetes, Skeletal muscle

A review of the identification and treatment of Helicobacter pylori infections (Review)

Mohammad Reza Mohammadi,[1,*] Abdolmajid Ghasemian,[2] Layegheh Daliri,[3]

1. Tarbiat Modares University
2. Tarbiat Modares University
3. Tarbiat Modares University

Introduction: Helicobacter pylori infection is one of the most common bacterial infections in humans. It affects about 50% of the human population (1). H. pylori was first identified in humans and cultured by Marshall and Warren (2). It is a slightly curved microaerophilic bacillus with several polar flagella. Although the organism was initially classified as a Campylobacter species, it could not be cultured on Campy BAP agar medium because it is sensitive to cephalothin

Methods: Herein, we used data published in various data bases searching the words “Helicobacter pylori”, “Identification” and “treatment”.

Results: Methods of identification of H. pylori are divided into two categories: invasive and non-invasive. Invasive methods detect bacteria directly from gastric biopsy but non-invasive methods examine different samples. The key to effective treatment for H. pylori infection is the use of combination therapy being similar to the treatment for bacterial meningitis or endocarditis. Although alternative therapies, including herbal remedies and probiotics, have been used to improve eradication, current treatments still rely on a combination of antimicrobial agents such as amoxicillin, clarithromycin, metronidazole, and levofloxacin, as well as antisecretory agents such as proton pump inhibitors.

Conclusion: Both invasive and non-invasive diagnostic methods are used for the identification of H. pylori. Combination therapies are more efficient to eradicate the bacterium

Keywords: H. pylori, treatment, metronidazole, amoxicillin, levofloxacin

A review of the use of stem cells in the treatment of reproductive disorders in infertile couples (Review)

Parmida Khanigavaei,[1,*] Mahnaz Nasimi,[2]

1. Hajar High School
2. Hajar High School

Introduction: Nowadays, infertility is a social problem and has created many problems for human societies. According to the World Health Organization. 10 to 15 percent of couples are infertile. Due to the importance of the subject, researchers made a lot of efforts regarding to the reduction of reproductive disorders. Stem cells are one of the ways to treat infertility. In this study, the effect of stem cells in the treatment of reproductive disorders in couples was investigated.

Methods: The present article was done by library method. Relevant information on the effect of stem cells in the treatment of reproductive disorders in men and women was searched from databases using the keywords stem cells, infertility, reproduction and treatment without time limit. Data analysis was performed qualitatively. Finally, 40 articles in English were used to organize the article.

Results: Extraction and differentiation of germ cells from various cellular sources including ovarian and uterine stem cells and spermatogonial stem cells in vitro conditions, by using effective factors in the process of cell differentiation, is an efficient method for infertility research.

Conclusion: Ovarian and testicular stem cells can have many applications in the treatment of reproductive disorders. Whereas laboratory culture conditions may not be able to imitate in vivo conditions completely, these methods can only enhance the hope of reaching adult germ cells in human models. Therefore, more research is needed to optimize the cultivation conditions in vitro.

Keywords: Infertility, Reproduction, Stem cells, Treatment

A review of web-based interventions in health indicators (Review)

Farzaneh Rassaf,[1,*] Zeinab Hamzehgardeshi,[2]

1. Midwifery Counseling, Mazandaran University of Medical Sciences, Sari, Iran ,
2. Department of Midwifery and Reproductive Health, Mazandaran University of Medical Sciences, Sari, Iran

Introduction: Introduction: Today, communication networks and data transmission have undergone a dramatic change in terms of quality and breadth; Health service delivery methods have also undergone significant changes, which have created a new concept called "e-health". The aim of this study was to evaluate web-based interventions to promote family health.

Methods: Materials and Methods: The present study is a multidisciplinary study. In this study, 320 articles were searched by electronic search by entering the desired keywords in Pubmed, Science Direct, Cochrane Library, SID, Magiran and Irandoc databases from the time period covered by these banks up to 2021 was obtained. Finally, Five web-based intervention studies from 2001 to 2021, which promoted family health, were reviewed.

Results: Results: Of the five studies, one was web-based middle-aged physical activity interventions, many of which did not express an initial interest in websites that had physical activity programs, and some said they would be interested if they had structured exercise programs. The second study was web-based mental health interventions and stated that the availability of tools and tools is problematic for very busy and busy end users. In the third study, an online survey was conducted to support mental health and well-being and showed that many people find these technologies targeted but in some cases were not seen as an alternative to traditional face-to-face treatment. In the fourth study, web-based virtual social intervention for students' mental health, there was a statistically significant decrease in scores of depression, stress and anxiety arose, also there were significant changes in consciousness and quality of life, but these factors did not change life satisfaction. In the 5th study, the evaluation and standardization of evaluation reports of web-based and mobile-based health interventions was performed and according to the results of the web-based physical activity intervention, it has a significant effect on improving physical activity and improving psychological well-being.

Conclusion: Conclusion: The results showed that with the increase of smart phones, websites and other wireless technologies, benefits of health services, the health of family members , and the use of health services in developing countries such as Iran is essential.

Keywords: Keywords: web-based, interventions, health

A scoping review on women's sexual self-efficacy (Review)

Zohreh shahhosseini,[1,*] sakineh ahmadi,[2]

1. Mazandaran university of medical science
2. Mazandaran university of medical science

Introduction: Sexual self-efficacy is a multidimensional construct that includes one's belief in one's abilities to have effective sexual function, be desirable for the spouse, and evaluate self-efficacy in sexual behavior. Understanding sexual self-efficacy is important in marriage which some women do not express it due to shame, but protest their sexual problems like anxiety, depressive symptoms, sleep disorders or gynecologic symptoms. Sexual self-efficacy plays a fundamental role in sexual decision making and eventually the result is prevention of high-risk sexual behavior and sexually transmitted infections. This review aims to discuss the effective, related factors , outcomes and identify effective interventions in women's sexual self-efficacy.

Methods: This study is a scoping review performed by searching for -women, sexual self-efficacy,self -efficacy- keywords in authoritative databases like PubMed, Scopus, Elsevier and Google Scholar. Among 110 articles related to the research topic,8 studies were obtained from 1997-2021 period and reviewed.

Results: According to the studies found, two studies evaluated effective and related factors in women's sexual self-efficacy, two studies discussed outcomes and four studies declared effective interventions on women's sexual self-efficacy. Results of this study showed that some main related factors to sexual self-efficacy are: 1)Socio-demographic factors: age, race, socioeconomic status, parental support, social support, religious obligations, negotiation skills, addicts, working hours, history of delivery, physical problem.2)Marital status factors: failure in marital, marital satisfaction, marital quality, marriage duration, intimacy. 3)Sexual history factors: sexual self-concept, sexual experience, confidence in sexual relationships, sexual activity, sexual self- schema, sexual adjustment, childhood sexual abuse, sexual disorders, sexual risk cognition, experiences of abuse or violence, partner's belief, experiences of sex-therapy training.4)Psychological factors: obsession, psychosis, anxiety, depression, paranoia, phobia, individual sensitivity, aggression .Young women have more sexual self-efficacy when they have greater autonomy and report partners to be more supportive and warmer, and less coercive and rejecting. It has been declared that one out of three women in worldwide experience sexual violence, Due to the association between sexual violence and sexual self-efficacy, health professionals may provide sexual education programs to increase sexual self-efficacy. Sexual

self-efficacy is generally positively related, either directly or indirectly, to high risk sexual behaviors in both the regular and casual sexual context, therefor despite what it is insinuated, high levels of sexual self-efficacy is not associated with taking less high risk sexual behaviors. There is a connection between pregnancy and sexual dysfunction; On the other hand, sexual self-efficacy is positively correlated with some sexual function subscales; Thus, sexual function in women can be enhanced by increasing women's sexual self-efficacy. It has been showed that some interventions like cognitive-behavioral therapy (CBT), pelvic floor muscle exercise can emphasize sexual self-efficacy in pregnant women and counseling and sleep improvement can improve sexual self-efficacy in other women.

Conclusion: According to the results of this review study, sexual self-efficacy has multidimensional factors that one of the most important issue is autonomy with partner. Sexual self-efficacy may contribute to lower sexual violence in women but it does not reduce high risk sexual behaviors. Understanding the importance and effective, related factors in women's sexual self-efficacy, can contribute to effective interventions in women and enhance their sexual self-efficacy.

Keywords: women. sexual self-efficacy. self-efficacy

A Stereological Evaluation on the Effect of L-carnitine on Histological Changes in Mice Ovary Following Autotransplantation (Research Paper)

Khadijeh Sanamiri,[1,*] Malek Soleimani Mehranjani,[2] Maryam Shahhoseini,[3] Mohammad Ali Shariatzadeh,[4]

1. Department of Biology, Faculty of Science, Arak University, Arak, Iran
2. Department of Biology, Faculty of Science, Arak University, Arak, Iran
3. Department of Genetics, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran
4. Department of Biology, Faculty of Science, Arak University, Arak, Iran

Introduction: Ovarian tissue transplantation is performed to preserve fertility in patients undergoing chemotherapy and radiotherapy. However, the ischemia-reperfusion injury which occurs after the ovarian tissue transplantation causes follicular depletion and apoptosis. L-carnitine has antioxidant and anti-inflammation properties and can therefore be used to improve follicular survival and ovarian structure following transplantation.

Methods: 18 Naval Medical Research Institute (NMRI) mice (4–5 weeks old) were divided into 3 groups (n=6): control, autograft and autograft+L-carnitine (200mg/kg daily intrapritoneal injections). 28 days after transplantation, ovaries were removed and studied stereologically. Data were analyzed using one-way analysis of variance (ANOVA) and Tukey test, and the means were considered significantly different at $P<0.05$.

Results: The mean umber of primordial, primary, and preantral as well as antral follicles significantly reduced in the autograft group compared to the control group, whereas these parameters were significantly higher in the autograft+L-carnitine group compared to the autograft group. The mean total volume of the ovary and the mean volume of the cortex and medulla decreased significantly in the autograft group compared to the control group. Meanwhile, a significant increase in the mean total volume of the ovary and the volume of the medulla and cortex was observed in the autograft+L-carnitine group compared to the autograft group.

Conclusion: Our results indicated that L-carnitine can ameliorate the ischemia-reperfusion injuries on the mice ovarian tissue following autotransplantation.

Keywords: Ovary, Transplantation, L-carnitine, Stereology

A Study of Serum Copper Level and Ceruloplasmin Activity in Patients Suspected to have Wilson's Disease, in Isfahan (Research Paper)

mohammad hossein Madahali,[1,*]

1.

Introduction: Diagnosis of patients suffering from Wilson's disease is very important in chinics for which the measurment of ceruloplasmine activity and copper levels in plasma and urine are usually used in medical laboratories. To study the distribwtion of patients with wilson's disease, all suspected patients who were admitted to the laboratory in the Biochemistry Dept. were investigated

Methods: Our results showed the absence of plasma ceruloplasmine activity in 13 percent of the patients, named absolute deficient, in which the concentration of copper in serum was 406 + 505 ug/100 ml. The 24 hr urinary copper in this group was 246.3 + 7401 ug/24hr. The plasma and urinary levels of copper in normal subjects were shown to be 70-160 Ug/100 ml and 0-70 ug/24 hr. respectively

Results: Ceruloplasmine level in 16 percent of patients, named partially deficient, was 401+106 mg/100. This group showed the plasma and urinary copper levels of 48.8 + 12 Ug/100 and 219.9+41 Ug/24 hr, respectively. The rest of the patients, 71 percent, appeared to have these parameters within the normal range

Conclusion: Thus the plasma and wrinary levels of ceruloplamine, serume copper and 24 hr urinary copper were found to be 25.1 + 106 mg/100, 138.3 + 15.2 Ug/100 and 39.0 + 901 Ug/24 hr, respectively

Keywords: copper ceruloplasmine wilson

A Study of the Effects of Nutrition on Human Cerebral Cortex (Review)

Ata Hafezi,[1,*] Matin Barzgar,[2] Amin Vafaei poursorkhabi,[3]

1. Azadegan High School
2. Azadegan High School
3. Azadegan High School

Introduction: Every day, humans eat three main meals that consist of nutrients and minerals with particular impacts on different organs of the body (e.g., brain). Each one of the three meals contains different nutrients that are considered the energy sources for the organs of our bodies such as our brains. The shortage or excess of these nutrients can cause diseases and disorders in the performance of the brain and other organs with potential destructive impacts. The brain consumes the largest portion of the consumed energy. Substances such as calcium, potassium, and sodium improve the performance of the brain and the nervous system, though their excess can bring about some disorders. The current article aimed to investigate the impacts of nutrition on the human cerebral cortex.

Methods: Nutrients contain such minerals as – among other things - magnesium, sodium, and potassium that have considerable effects on the performance of the cerebral cortex. For instance, sodium and potassium are considered the neurotransmitters of synapses and play an important role in the performance of the cerebral cortex. The shortage of sodium results in exhaustion, lethargy, and even spasm, and its overconsumption can increase blood pressure and harm other parts of the body. Potassium also plays a key role in controlling blood pressure and control the amount of sodium. Its shortage can increase sodium, while its excess can reduce the rate of sodium. Moreover, magnesium and lithium play an important role in the prevention of depression and bipolar disorder. In addition to minerals, proteins play a key role in the cerebral cortex. For instance, dopamine and serotonin are neurotransmitters that are derived from two amino acids called tyrosine and tryptophan, respectively. The most important vitamin concerning the performance of the cerebral cortex is B12, the shortage of which can lead to mental deterioration. Carbohydrates and fats are also quite important in the provision of energy for the cerebral cortex, and the brain cannot function without them.

Results: Nutrition plays a key role in the performance of the cerebral cortex and can have multiple direct and indirect effects on the cerebral cortex. Nutrients that can have direct impacts on the cerebral cortex include unsaturated fatty acids such as omega 3, 6, and 9 that can assist in the development of the cerebral cortex, increase consciousness and the performance of the cerebral cortex, and improve memory. Furthermore, since

lycopene fights free radicals in the body and prevents the destruction of brain cells, it plays a key role in the well-being of the brain. Some vitamins such as C and K are quite important in the improvement of brain function and the enhancement of intelligence particularly among children and the newborn. Vitamin B4 is effective in the prevention of brain deterioration, as well. On the other hand, some substances have indirect impacts on the cerebral cortex. For instance, iron is a mineral that plays a major role in the performance of the brain. The shortage of iron brings about multiple problems for the body. Its shortage can lead to issues such as anemia, fatigue, hypoxia, and exhaustion. When the oxygen level of the body decreases due to the lack of iron, the cerebral cortex (as the organ that receives the largest portion of the oxygen in the body) suffers hypoxia and cannot continue its function. Moreover, the shortage of copper in the body prevents the production of antioxidants. Then, antioxidants such as vitamin K and lycopene are not absorbed well in the body, and this can harm the memory function of the brain. Another important mineral that is useful for the brain is zinc. It assists nerves and improves recall.

Conclusion: Nutrition and the nutrients that are consumed play a major role in the performance of the cerebral cortex. Fatty acids are quite helpful in the performance of the cerebral cortex and the enhancement of memory. In addition, vitamins C, K, and B4 are effective in the enhancement of memory. Moreover, iron and copper play important roles in supplying oxygen to the cerebral cortex and producing antioxidants. The shortage of the above substances can lead to brain deterioration, hypoxia in the cerebral cortex, and other issues.

Keywords: Cerebral Cortex, Brain, Nutrition ,Nerve

A survey on frequency of BK virus genotypes in renal transplant recipients in three hospitals in Tehran,2019-2020 (Research Paper)

Maryam Ghotbi,[1] Farhad Rezaei,[2,*] Talaat Mokhtari azad,[3] Nazanin zahra Shafiei,[4] Najmeh Parhizgari,[5]

1. Virology Department, School of Public Health (SPH), Tehran University of Medical Sciences (TUMS), Tehran, Iran
2. Virology Department, School of Public Health (SPH), Tehran University of Medical Sciences (TUMS), Tehran, Iran
3. Virology Department, School of Public Health (SPH), Tehran University of Medical Sciences (TUMS), Tehran , Iran
4. Virology Department, School of Public Health (SPH), Tehran University of Medical Sciences (TUMS), Tehran, Iran
5. Virology Department, School of Public Health (SPH), Tehran University of Medical Sciences (TUMS), Tehran, Iran

Introduction: The BK polyomavirus (BKPyV), is a non-enveloped icosahedral deoxyribonucleic acid (DNA) virus and represents a discrete species within the genus Polyoma virus of the family of Polyomaviridae, is widespread in the human population. BKPyV is a circular double-stranded DNA virus that encodes for seven proteins, of which Viral Protein 1 (VP1), the major structural protein, has been extensively used for genotyping. The primary BKV infection is occurred during childhood then the virus could be latent through life especially in the kidneys and urinary system. It became reactive after an immunocompromised status, such as pregnancy or transplantation. Since the discovery of BK Virus (BKV) was first isolated from the urine of an immunocompromised renal transplant patient in 1971, it became a growing challenge in the renal transplant field. BKPyV has been linked mostly to polyomavirus-associated hemorrhagic cystitis, in allogenic hematopoietic stem cell transplant, and polyomavirus-associated nephropathy in kidney transplant patients. BKV infection in renal transplant (RT) recipients can cause BKV nephropathy (BKVN) that has been recognized as an important cause of silent loss of kidney transplant function in up to 50% of kidney recipients. BKV isolates are classified into four subtypes (I–IV) using serological or genotyping methods, and subtype I is further divided into four subgroups, Ia, Ib-1, Ib-2, and Ic, based on DNA sequence variations. Human BK polyomavirus (BKPyV) prevalence has been increasing due to the introduction of more potent immunosuppressive agents in transplant recipients, and its clinical interest. The prevalence BKV in RT recipients remain to be clarified in the Iranian population.

Methods: Blood samples were collected from 250 kidney transplant recipients undergoing surgery at imam Khomeini, milad and shariati hospital in Tehran province between 2019 and 2020. The extracted DNA was amplified by

Polymerase Chain Reaction (PCR). PCR products were resolved by 1% agarose gel electrophoresis Bands corresponding to BKV viral capsid protein VP1 product and subtype of each positive sample was determined by using sequencing methods.

Results: Infection with the human polyoma BK virus was studied in 250 immunosuppressed renal transplant patients. BK virus was detected in 13 of 250 (5.2%) patient's serum but Only 9 positive samples were phylogenetic. All 9 complete BKV VP1 gene sequences retrieved from GenBank were aligned. A phylogenetic tree was then constructed in order to cluster all 9 strains according to their BKV subtype which resulted in subtype I was found in the serum of 89% (8/9) and subtype IV in 11%(1/9).

Conclusion: It is concluded that PCR for BK virus DNA in serum is useful both for identifying transplant recipients at risk for BK virus nephropathy and for monitoring the response to therapy and Testing for BKV DNA in urine and serum is a noninvasive early detection assay. Subtype I was the major subtype throughout the studied regions, and subtype IV was prevalent only in Asia and Europe. The VP1 region was highly polymorphic and 22 "hot spots" of sequence variability were noted.

Keywords: BK, BK virus, PCR, Phylogeny

A systematic review on the herbal treatment of primary dysmenorrhea (Review)

Zeinab Sattarivand,[1,*]

1.

Introduction: Primary dysmenorrhea is a painful experience, highly prevalent among women, and it is defined as painful menstruation. This is often sufficiently severe that it prevents a woman from performing normal activities and it is a source of recurrent disability for a significant number of women in their early reproductive years. Primary dysmenorrhea is caused by excess prostaglandin F2α (PGF2α) produced in the endometrium. It can be accompanied by various symptoms such as nausea, diarrhea, vomiting, headache, and dizziness. Patients with primary dysmenorrhea generally experience exceptional pain relief through the use of nonsteroidal anti-inflammatory drugs (NSAIDs), which are prostaglandin synthetase inhibitors. However, these drugs are now rarely used because of their potential association with life-threatening cardiovascular and gastrointestinal (GI) effects. Studies suggest that some herbal treatments can provide pain relief comparable to that offered by NSAID therapy without the systemic side effects that may occur with these drugs. In this paper, a systematic review was conducted to evaluate the efficacy of herbal medications in the treatment of primary dysmenorrhea.

Methods: Five databases were used in this study: Google Scholar, Scientific information database (SID), ResearchGate, PubMed, and ScienceDirect. The following search terms were used: (Primary dysmenorrhea OR Dysmenorrhea OR Painful menstruation) AND (Herbal medicine treatment OR Herbal medicine OR Medicinal plants). NO language limitations were used.

Results: This review includes 11 papers, 4 of which on comparison of the efficacy of herbal medications with nonsteroidal anti-inflammatory drugs such as mefenamic acid, 4 on the effects of herbal treatment without applying any NSADs, one on the effect of rose essential oil on dysmenorrhea, one on the comparison of the effect of ginger and zinc sulfate on primary dysmenorrhea, and one on assessing medicinal plants as complementary medicine in primary dysmenorrhea. These studies looked into the use of plants such as Cinnamomum verum (cinnamon), Zingiber officinale (ginger), Salvia officinalis (common sage), Menta piperita (peppermint), Foeniculum vulgare (fennel), Teucrium polium (felty germander), Matricaria chamomilla (chamomile), Vitex angus-castus (vitex), Darcocephalum (dragon head), Anethum graveolens (dill) seeds, Thymus vulgaris (thyme), Cuminum cyminum (cumin), Amomum subulatum (black cardamom). Sample sizes in the studies ranged from 44 to 150 patients. The controls were given placebo capsules (containing starch (,

placebo drops, diclofenac sodium, and mefenamic acid capsules, while individuals in the case groups were given fennelin oral drops, agnugol tablets, chamomile capsules, cinnamon capsules, Darcocephalum and salvia officinalis decoctions, peppermint capsules, diclofenac sodium with rose essential oil aromatherapy, and ginger capsules. The length of treatments in the studies ranged from one to seven months and the measures most commonly used in the studies were the visual analogue scale and clinical efficacy. No specific complications were reported.

Conclusion: From 11 papers in this review 4 found that the efficacy of herbal treatments is comparable or better than to that offered by NSAID treatments, and 7 papers confirm that medicinal plants are highly effective on primary dysmenorrhea. In many cases herbal medications appear to have far less complications than NSAIDs. Herbal treatments seem to suppress pain and reduce the clinical symptoms of dysmenorrhea by decreasing the level of prostaglandins, enhancing circulatory flow through the uterine pathway, mediating nitric oxide, and blocking the calcium channel. Further trails are required to confirm the benefits of mentioned medicinal plants and ensure the absence of complications.

Keywords: Primary dysmenorrhea, herbal treatment, medicinal plants

Adherence to a DASH dietary pattern in correlation with breast milk composition and psychological performance in lactating women (Research Paper)

Samira Karbasi,[1,*] Afsane Bahrami,[2] Asghar zarban,[3]

1. Student Research Committee, Birjand University of Medical Sciences, Birjand, Iran
2. Cellular and Molecular Research Center, Birjand University of Medical Sciences, Birjand, Iran
3. Department of Biochemistry, Faculty of Medicine, Birjand University of Medical Sciences, Birjand, Iran

Introduction: Mother milk is nutrient-rich and essential for a baby's health through its role in nutrition and immunological development. This study aimed to find the association between adherence to a DASH dietary pattern and breast milk composition and psychological performance in both mothers and their infants.

Methods: A total of 700 milk samples were obtained from 340 women who were randomly selected from four different areas. The dietary intakes of the study mothers were estimated by a validated food frequency questionnaire (FFQ) including 65 food items. Psychological functions of subjects were assessed by standard and valid instruments. The total antioxidant statues (TAS) of milk samples were evaluated by the ferric reducing/antioxidant power assay (FRAP), 1, 1-diphenyl-2-picrylhydrazyl (DPPH) radicals, malondialdehyde (MDA) and thiol assay. Also, using commercially available kits, the total protein, calcium (Ca), and triglyceride contents of milk were determined.

Results: Subjects with the highest tertile of DASH DP had higher scores of milk DPPH, thiol and calcium compared to those in the first tertile ($p< 0.05$). Milk MDA was significantly lower in the 3rd tertile of DASH DP versus the 1st tertile ($P<0.05$). Mothers with the third tertile of DASH DP had significantly lower sleep latency compared to those in the first tertile ($p<0.05$). On the other hand, the increase in Pittsburgh Sleep Quality Index (PSQI), and sleep efficiency were positively linked to the highest tertile DASH DP. Total infant sleep disorders with 3rd tertile of DASH DP were significantly lower compared to those in the first tertile ($p<0.05$).

Conclusion: Our results demonstrated that a DASH diet could significantly increase milk oxidant/antioxidant status and decrease sleep problems in both mothers and their infants. Furthermore, prospective studies are required to validate these results.

Keywords: DASH dietary pattern, total antioxidant statues, breastfeeding mothers, psychological performance

Advances in viral therapy in human cancers (Review)

Piruz Shadbash,[1] Seyed Reza Mohebbi,[2,*] Seyed Masoud Hosseini,[3] Seyed Amirmohammad Seyed Mirzajani,[4] Shabnam Kazemian,[5] Hamid Asadzadeh-Aghdaei,[6]

1. Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences
2. Research Center for Gastroenterology and Liver Diseases, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
4. Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences
5. Research Center for Gastroenterology and Liver Diseases, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
6. Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Introduction: In recent years, oncolytic virus therapy has appeared as a promising anti-cancer treatment. The idea of using viruses as a cancer therapy was formed in the 1950s. Oncolytic virotherapy is discussed as a key factor in modern immunotherapy. Oncolytic viruses selectively replicate in cancer cells and destroy them without damaging normal cells. Oncolytic viruses invade and activate tumor immune cells by promoting the release of large amounts of tumor antigens and cytokines.

Methods: Although, there are multiple challenges to exploiting the potential of oncolytic viruses, like the lack of biomarkers for accurate treatment, the difficulty of systemic administration due to the presence of neutralizing antibodies in popular oncolytic viral vectors in human serum.

Results: Many cancer patients have been treated with oncolytic viral drugs that are administered in almost every possible route, and some have developed tumor regression at various times. The M1 strain, isolated in the 1960s on the Chinese island of Hainan, belongs to the alphavirus genus Togaviridae family.

Conclusion: During the development of the M1 virus, many challenges have been addressed and numerous biomarkers have been recognized for accurate treatment. Systemic administration of M1 is appropriate due to the very low percentage of neutralizing antibodies in the general population.

Keywords: Oncolytic viruses, Biomarkers, Neutralizing antibodies, M1 virus

Allelopathy: A potent potential in new drug discovery (Review)

Hamideh Bakhshayeshan-Agdam,[1,*] Seyed Yahya Salehi-Lisar ,[2]

1. Department of Plant Sciences, Faculty of Natural Sciences, University of Tabriz, Tabriz-5166616471, Iran
2. Department of Plant Sciences, Faculty of Natural Sciences, University of Tabriz, Tabriz-5166616471, Iran

Introduction: Allelopathy is one of the most important interaction among organisms, which is sub-discipline of chemical ecology. Indeed, it is ecological behavior which evolved during natural selection. The allelopathy phenomenon is triggered by production and releasing of certain compounds called allochemicals that are species- and tissue- specific compounds, mainly producing as secondary metabolites. Allelochemicals that are produced chiefly by plants, bacteria, fungi, lichens, micro- and macro-algae, viruses, and animals could be a potent source of compounds for discovering new drugs.

Methods: The majority of compounds that used in traditional medicine are allelopathic compounds. Hence, the current review focuses on introduce allelopathy phenomenon and related compounds (allelochemicals) as novel and natural source for drug discovery. This review provides an opportunity to reveal allelopathy usage in pharmacy.

Results: In fact, allelopathy is an action against diseases, and organisms use it to protect themselves against biotic stresses. Today, it is safe to say that most of the natural compounds used in traditional and even modern medicine for remedy are allopathic compounds. Plant extracts, which are now widely used, often contain large amounts of allelochemicals. Many allelochemicals are found in cosmetic products such as rosemarinic acid and many phenolic compounds. Allelopathic compounds are a rich source of unknown compounds for the production of new drugs. Dramatic increases in natural drugs production have been observed from the latter half of the twentieth century owing to the increasing reliance on traditional medicine and natural products. The use of natural drugs by humans is increasing day by day and there is a need for an infinite source. Although the natural drugs are the good option to disease remedy, but they are not devoid of some drawbacks such as use limitation, emergence of drug-resistant diseases, and so on, have led scientists to seek and discover alternative resources for new drugs. Allopathic plants and microorganisms could be good sources for finding new drugs. Nowadays, there are limited studies on allelopathy and its potential in biomedicine, which is increasing day by day. One of the studies that has been done is the effect of redroot pigweed allelopathy on leukemia cancer. The allelochemical compounds of this plant have the power to inhibit growth and

proliferation of cancer cells. There are several similar examples in this regard that including allelopathic plants, bacteria, and even aquatic organisms.

Conclusion: Overall, the study results of allelopathy effects on diseases such as cancer are so significant that investigate to allelopathy in biomedicine and pharmacy is inevitable. Definitely, targeted studies of allelopathy for drug production would herald a new revolution in the pharmaceutical industry.

Keywords: Allelopathy, pharmacy, allelochemical, drug discovery, natural drug

Alteration of NT4 gene expression and depression- like behaviors during copper toxicity in the brain of rats under vitamin C treatment (Research Paper)

Sama Radbin,[1,*] Homeira Hatami,[2] Hatam Ahmadi,[3]

1. Department of Animal Biology, Faculty of Natural Sciences, University of Tabriz, Tabriz, Iran
2. Department of Animal Biology, Faculty of Natural Sciences, University of Tabriz, Tabriz, Iran
3. Department of Basic Sciences, Farhangian University, Tehran, Iran

Introduction: Copper is one of the essential elements of the body. The amount of copper in human brain tissue is about 3.1 mg/g. In mice, it is 5.5 and in rats, it is 0.1 mg/g. But excess amounts of copper can damage the brain by causing oxidative stress. Excessive increase or decrease in copper causes neurodegenerative diseases. To counteract this effects, the use of antioxidants is recommended. Ascorbic acid (vitamin C) is antioxidant and it can stand against the effects of oxidative stress. Neurotrophin-4 (NT-4) is a member of a family of neurotrophic factors, the neurotrophins that control survival and differentiation of vertebrate neurons. Neurotropic factor 4 (NT4) is involved in different neural process. Studies show that neurotrophin 4 is a protective and survival factor against neurotoxicity. So in this study, we evaluated the NT4 gene expression alterations and locomotor activity in rats following copper toxicity and treatment with vit C.

Methods: Twenty four male Wistar rats were randomly assigned into four groups (n=6). Control, copper sulfate (10 mg/kg; i.p), vitamin C (100 mg/kg; i.p), copper sulfate +vitamin C (100mg/kg; i.p) doses for 10 days. The exploratory behavior and depression- like behaviors of animals were assessed by open field test on the first, fifth and tenth days of the injection. After receiving treatments, the animals were decapitated and their cerebral hemispheres were removed and the expression of NT4 gene assayed using RT- PCR. One-way ANOVA were used for data analyzing.

Results: Data analyzing showed that the duration of presence in the central part of the open field device in copper sulfate group and vitamin C group and copper sulfate + vitamin C group, significantly decreased compared to the control group ($p<0.001$). There is no significant difference between copper sulfate receiving group and vitamin C group and copper sulfate + vitamin C group ($p>0.05$). And there is no significant difference between vitamin C group and copper sulfate + vitamin C group ($p>0.05$). The frequency of entry of the group receiving copper sulfate and vitamin C group and copper sulfate + vitamin C group in the central part, significantly decreased compared to the control group ($p<0.001$). There is no significant difference between copper

sulfate receiving group and vitamin C group and copper sulfate + vitamin C group ($p>0.05$). And there is no significant difference between vitamin C group and copper sulfate + vitamin C group ($p>0.05$). The NT4 gene expression decreased in the copper sulfate group and vitamin C group and copper sulfate + vitamin C group compared to the control group ($p<0.001$). There is no significant difference between copper sulfate receiving group and vitamin C group and copper sulfate + vitamin C group ($p>0.05$). And there is no significant difference between vitamin C group and copper sulfate + vitamin C group ($p>0.05$).

Conclusion: Behavioral data analyzing showed copper toxicity induced depression like behaviors in rats in a way rats the rats did not want to explore and search the central part of open field device. Most of animals crawled in the corners of open field device. Interestingly vit C did not improved their behaviors. Also molecular data analyzing showed that the level of NT4 gene expression decreased during copper toxicity and vit C treatment was not able to approach it to the control level. Good coordination between behavioral data analyzing and molecular data analyzing was seen.

Keywords: Copper sulfate, Vit C, Neurotrophin-4 gene expression

Amelioration of Sodium Valproate Reproductive Toxicity by Curcumin in Male Mice; Involvement of Mitochondrial Oxidative Stress (Research Paper)

Fatemeh shaki,[1] Moein Shaneh,[2,*] Nasibeh Hematib,[3] Seyed Mohammad Reza Seyed Moghadam,[4]

1. Department of Toxicology and Pharmacology Mazandaran University of Medical Sciences
2. Student Research Committee, Mazandaran University of Medical Sciences, Sari, Iran
3. Student Research Committee, Department of Toxicology and Pharmacology Mazandaran University of Medical Sciences,
4. Student Research Committee, Department of Toxicology and Pharmacology Mazandaran University of Medical Sciences,

Introduction: Sodium valproate (SV) is a well-known drug that is used in the treatment of several disorders such as tonic-clonic convulsions, infantile spasms, cluster headache, migraine prevention, schizophrenia, major depression, and behavioral disturbance in dementia. The pharmacologic mechanism of SV is through the clogs of the voltage-dependent sodium channels and also amplification of the gamma-aminobutyric acid (GABA)-ergic system as well as increasing GABA concentration(1). Long-term consumption of SV is associated with diverse adverse effects on several organs in the body including brain, liver, kidney, and reproductive system(2, 3). Experimental animal studies have documented infertility and testicular atrophy after prolonged exposure to SV(3). Furthermore, evidence suggested that chronic SV therapy decreases testosterone level and declines sperm quality in epileptic men who received SV treatment(4). Based on reports of mechanistical studies, induction of oxidative stress and mitochondrial damage are the main causes of SV-induced testicular toxicity(5). Oxidative stress results from an imbalance between the over-production of reactive oxygen spices (ROS) and neutralizing effects of endogenous antioxidants in the body(6). Giovana et al showed that oral administration of SV (400 mg/kg) for 28 days, caused testicular oxidative damage, which was exhibited by increasing lipid peroxidation, protein oxidation, and glutathione (GSH) depletion in mice testes(5). It was also shown that SV can affect mitochondrial function. Mitochondria, as the main site of cellular ROS generation, are the energy production center for all biochemical reactions, including spermatogenesis. It also provides the energy needed for sperm motility. Therefore, any disturbance in mitochondrial function such as increased ROS production, is closely related to poor sperm quality and motility(7). Due to the role of oxidative stress in triggering SV-induced toxicity, it is suggested that compounds with free radical scavenging or antioxidant effects can be beneficial for preventing SV testis toxicity. Curcumin (CUR) is a natural

antioxidant compound, which is derivate from turmeric (Curcuma longa L.) root. It is used as popular spice in the food industry (8). CUR has many beneficial medicinal properties such as anti-inflammatory, anti-cancer, antifungal, anti-ischemic, anti-tumor, analgesic, anti-arthritic and anti-mutagenic effects(9, 10). Previous studies exhibited protective effects of CUR against testicular oxidative damage induced by various toxic chemicals(11, 12). For example, Momeni et al reported that CUR administration ameliorated doxorubicin-induced testicular oxidative damage by reducing lipid peroxidation, DNA oxidation, increasing superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) activity as well as restoring GSH storages in testis tissues of rats(11). So, in this study, we evaluated the possible protective effects of curcumin against the SV-induced testicular toxicity in mice via focusing on the mitochondrial oxidative damage.

Methods: In this study, 36 adult male mice were divided into six groups: control, SV (500 mg/kg, i.p), SV + three dose of CUR (25, 50 and 100 mg/kg, i.p) and CUR alone (100 mg/kg, i.p). The treatments were delivered for 6 weeks. Then, the animals were sacrificed and testis tissues were separated and several factors including oxidative stress markers and mitochondrial toxicity were evaluated. Also, epididymis was separated for evaluation of sperm quality factors.

Results: SV exposure increased levels of protein carbonyl, malondialdehyde, and GSH depletion in testis tissue. Also, it caused mitochondrial dysfunction, mitochondrial membrane potential collapse, and mitochondrial swelling in testis isolated mitochondria. Furthermore, a decrease in sperm count, motility, and normal morphology were observed in SV- treated mice. Significant histopathological changes were observed after injection of SV. Interestingly, CUR ameliorated SV-induced testis oxidative stress, mitochondrial damage, and improved histopathologic lesions. Also, co-administration of CUR with SV resulted in restoring sperm normal characteristics in mice.

Conclusion: Taken together, in the current study, CUR administration showed a positive impact on SV-induced reproductive toxicity through ameliorating oxidative stress and mitochondrial toxicity. So, it is suggested CUR can be used as a supplement in the patient who is under prolonged SV treatment.

Keywords: Sodium valproate; Curcumin; Oxidative stress; Mitochondria; Testis.

An in-silico study of natural Tyrosinase inhibitors (Research Paper)

pardis zamani,[1,*]

1. isfahan university

Introduction: Tyrosinase is a copper-containing oxygenase involving in melanin synthesis and could cause hyperpigmentation and browning in human skin, fruits, and vegetables. Inhibitors of this metalloenzyme have various applications in pharmaceutical biotechnology, agricultural industry, and cosmetics as skin-whitening agents. Multiple traditional herbals are known as potent drugs to prevent the enzyme from working normally.

Methods: In the current article, we provided a library of some flavonoids as natural inhibitors and conducted a study on tyrosinase through homology modeling and molecular docking techniques to provide the probable interaction and binding energy of the selected compounds. Also, Kojic acid, a proven inhibitor of tyrosinase, was used as a positive control.

Results: Our post docking analysis showed among all tested compounds, Glabrene, Artocarpesin, Norartocarpetin, and Steppogenin displayed the lowest binding energies that show their remarkable inhibitory effect against Tyrosinase.

Conclusion: These in-silico results recommended four flavonoids as potent candidates of melanogenesis medication for further inference in the drug development process.

Keywords: Molecular docking, flavonoid, inhibitors, pharmaceutical herbs, Tyrosinase

An Insight Into The Viral Interleukin-6 Encoded By Human Herpesvirus 8 (Review)

Hassan Karami,[1,*]

1. Department of Virology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

Introduction: Human Herpes Virus 8 (HHV-8) is an oncogenic, lifelong persistent, and lymphotropic pathogen in association with different types of malignancies and disorders. This virus encodes a unique gene product, Viral Interleukin-6 (vIL-6), to induce tumorigenesis by modulating cell signaling pathways. This study aimed to review the structure, function, and pathogenic role of vIL-6 in a brief description.

Methods: For the present review, three scientific databases including PubMed, Google Scholar, and ScienceDirect were searched since 1987 using the following keywords: “Viral Interleukin-6” and “Human Herpesvirus 8”.

Results: Viral Interleukin-6 (vIL-6) is an intracellular growth factor being homolog counterpart of human IL-6 (hIL-6). This protein which is produced by the ORF-K encoding gene of HHV-8 is similar to its equivalent in humans (hIL-6) in both structural and functional properties. However, there are some differences between these two proteins such as the receptor they use and their affinity in receptor binding. vIL-6 is a three-dimensional protein which structurally consisting of 204 amino acids with 22.6 kDa in molecular weight and four conserved residues of cysteine responsible for forming four-helical bundles. Functionally, this viral cytokine is an activator for transcription factors and signal transduction by tetrameric complexes through A broadly expressed GP130 direct interaction and independent of the presence of IL-6 receptor. This activation may induce cell proliferation, migration, invasion, angiogenesis, and hematopoiesis leading to metastatic virus-associated malignancies and lymphoproliferative disorders. Moreover, this protein has shown anti-apoptotic features that is critical for the survival of those cells which are HHV-8-infected. Generally, vIL-6 is a lytic gene; however, it may also be expressed during the latency phase of infection at a low detectable level. This protein may also regulate the immune system as is able to modulate the functional immunity like hIL-6 induction.

Conclusion: Viral Interleukin-6 (vIL-6) is a key virus-derived cytokine that playing a role in the pathogenesis of HHV-8-associated tumors and diseases. In this context, some interventions such as vIL-6 neutralization may inhibit the activation of cell signaling mediated by this viral mediator.

Keywords: Viral Interleukin-6 (vIL-6), Human Herpes Virus 8 (HHV-8)

An investigation into polyphenols effect on the cell viability and Nrf2 mRNA level in HepG2 cancer cell line (Research Paper)

Delaram Moghadam,[1] Reza Zarei,[2] Rozita Ghojoghi,[3] Fakhraddin naghibalhossaini,[4,*]

1. Shiraz University of Medical Sciences
2. Shiraz University of Medical Sciences
3. Shiraz University of Medical Sciences
4. Shiraz University of Medical Sciences

Introduction: Natural phenolic compounds are abundant secondary metabolites of plants. Over the last decades, polyphenols have attracted attention due to their potent antioxidant, anti-infection, anti-inflammation, immunity enhancement, and anticancer properties (1). Kuromanin chloride, gallic acid, and resveratrol are natural polyphenols of the flavonoids, phenolic acids, and stilbenes classes (2-4). Current evidence suggests that polyphenols exert their anticancer effects through several mechanisms including, inhibition of cell cycle arrest, apoptosis, induction of antioxidant enzymes, and autophagy (5). Several studies indicated that polyphenols modulate the nuclear factor erythroid 2-related factor 2 (Nrf2) signaling pathway. Nrf2 is a crucial transcription factor involved in cell protection against oxidative stress (6). Indeed, induction of various cytoprotective genes by Nrf2 leads to the protection of cells against exogenous or endogenous oxidative stress (7). However, Nrf2 activation was found to promote cancer development and malignant progression (8). The present study compared the effect of three polyphenols (kuromanin chloride, gallic acid, and resveratrol) on Nrf2 gene expression and cell viability in the HepG2 liver cancer cell line.

Methods: HepG2 hepatoma cell line was grown in RPMI-1640 medium with 10% FBS, and 1% Penicillin-Streptomycin and incubated under standard conditions. Cells were treated for 72h with an increasing concentration of each of the three polyphenols. After a 72h incubation period, cells were harvested and total RNA was extracted using RNX- Plus reagent (Sinaclon, Iran). The RNA concentration and purity were assessed by NanoDrop ND-2000. The cDNAs were synthesized using EURX one-Step RT-PCR Kit (Gdansk, Poland) and amplified by qPCR SYBR Green Master Mix (AddBio, Korea) on StepOn Real-Time PCR System. In addition, cell viability was determined by trypan blue exclusion assay.

Results: The results of the present study showed that kuromanin chloride and resveratrol significantly upregulated expression of Nrf2 gene dose-dependently in HepG2 cells, compared with the control group. The highest concentration of resveratrol (40 μM) increased the expression of Nrf2 by 5.5 fold ($p< 0.001$) compared to the non-treated control group. Concentrations of

10, 20, and 40 µM kuromanin chloride increased Nrf2 gene expression by 2.6, 3.6, and 4.9 fold, respectively. Low concentrations of gallic acid (10 and 20 µM) dramatically increased Nrf2 gene expression by 4.4 and 3 fold, respectively. However, no significant change was observed in 40 µM gallic acid. As shown by the results, all polyphenols significantly reduced cell viability and cell number compared with the control group. Gallic acid reduced cell viability and cell number more efficiently in comparison to resveratrol and kuromanin chloride. Compared to the control group, the highest concentration of gallic acid (40 µM) reduced cell number and cell viability by 73% ($p < 0.001$) and 13% ($p < 0.001$), respectively.

Conclusion: Our current study showed that all three polyphenols reduced the cell proliferation and viability of HepG2 cells. All three polyphenols increased Nrf2 gene expression, except the highest tested concentration of gallic acid (40 µM). Gallic acid is a dietary polyphenol with antioxidant and pro-oxidant characteristics (1). Gallic acid exhibited a stronger inhibition effect on the cell proliferation of HepG2 cells compared to resveratrol and kuromanin chloride. This effect of gallic acid may be due to its pro-oxidant properties. Many studies indicated the contradictory role of Nrf2 in cancers. Nrf2 expression protects both cancer and normal cells against oxidative stress. Indeed, Nr2 overexpression leads to enhancement of cancer cell proliferation through upregulation of metabolic genes (2). Further in-vivo and in vitro studies are required to shed light on the anticancer properties of different polyphenols against hepatocellular carcinoma through the induction of the Nrf2 pathway.

Keywords: Gallic acid, Kuromanin chloride, Liver cancer, Nrf2, Resveratrol

An Investigation into the Effects of Stem Cells on the Treatment of Human Liver Cirrhosis (Review)

Niyayesh Zabeti,[1,*] Sayyedeh Yasaman Mousavi,[2] Najmeh Zaree,[3]

1. Farzanegan Gifted and Talented (GT) High school
2. Farzanegan Gifted and Talented (GT) High school
3. Faculty Member, Shiraz University of Medical Sciences

Introduction: Liver cirrhosis is one of the main causes of death, which from the hygienic point of view imposes a high cost on the health care system throughout the world. Presently, the only effective treatment is liver implantation. However, due to limitations and numerous side effects, new alternative methods are required to treat the patients suffering from liver cirrhosis. Findings obtained from research illustrates that the use of hematopoietic stem cells, mesenchyme stem cells, and bone marrow stems cells has been considered for the development of liver cirrhosis treatment.

Methods: This review study was conducted using ten articles that were the result of an analytical review of forty-eight articles obtained from reliable websites. The review was done by searching for such key words as bone marrow stem cells, liver cirrhosis and cell therapy. The articles used were obtained from such scientific sites as PubMed, SID, Google Scholar, Scopus, and SiteSeer.

Results: Evidence suggests, using mesenchyme stem cells as a potential therapy, is more effective than liver-regenerating drugs, which happens through bone marrow or hematopoietic stem cells.

Conclusion: Evidence suggests, using mesenchyme stem cells as a potential therapy, is more effective than liver-regenerating drugs, which happens through bone marrow or hematopoietic stem cells.

Keywords: bone marrow stem cell, mesenchymal stem cell, cell therapy, liver cirrhosis.

An overview of stem cell (Review)

Amir Shourideh,[1,*] Ardavan Amanat,[2]

1. Eastern Mediterranean University
2. Iran University of Medical Sciences

Introduction: In recent years there have been many advances in stem cell research, which is a promising new therapeutic strategy for incurable diseases. These cells are found in all multicellular organisms and have the ability to divide and differentiate into a variety of specialized organisms. Cell types and can also replace lost and damaged cells. The self-renewing property of stem cells and their effectiveness have been suggested as promising future uses of these cells in regenerative medicine, cell therapy, and drug research. autologous and non-autologous stem cells. Stem cell therapy has some limitations, so further research is essential to improve our biological understanding. This article provides an overview about importance and treatments of stem cell.

Methods: This study is a review by analyzing articles from dependable scientific databases including Google Scholar, ScienceDirect, PubMed, and Scopus.

Results: In theory, stem cells or their derivatives can be used to restore any tissue in the body that has been lost or damaged by disease or injury. Examples of these potential treatments currently under investigation are: Restoring bone growth after bone injury, restoring vision in retinal disease, restoring nerve cell function in spinal cord injury, Parkinson's and Huntington's disease and Restoring heart tissue after a heart attack. Many stem cell treatments are unproven and still experimental. While stem cells have great potential to help people in the future, they can also be dangerous if used incorrectly. They can get into the wrong parts of the body and cause problems, and they can also be dangerous. they have the ability to turn into tumors. In recent years, there have been many "stem cell clinics" in the United States and around the world offering various "stem cell treatments" that are not scientifically proven or regulated by the US Food and Drug Administration (FDA). For the most part, these clinics claim to use stem cells from their own body fat, bone marrow, and blood, although some use cells from amniotic fluid, placental tissue, umbilical cord tissue, and even unknown sources from other donors' cells. The cells used are actually stem cells. These clinics tend to false advertising to the public with the promise that stem cell treatments can improve cosmetic appearance and help a variety of conditions ranging from arthritis to autism. Guideline development process to regulate these clinics more strictly.

Conclusion: Doctors and scientists love stem cells because they could help in many different areas of health care and medical research. Studying stem cells can help explain how serious diseases such as birth defects and cancer develop. Stem cells may one day be used to make cells and tissues for the treatment of many diseases; for example, Parkinson's disease, Alzheimer's disease, spinal cord injury, heart disease, diabetes, and arthritis.

Keywords: Stem Cells, Biology, Clinical Application

An overview of the health benefits of kombucha nutritional compounds and metabolites (Review)

Ali Akhavan sepahi,[1] Mohaddeseh Larypoor,[2,*]

1. Undergraduate student in biotechnology, Science Campus, Faculty of Biological Sciences, University of Tehran, Iran
2. Department of Microbiology, Faculty of Biological Sciences, Islamic Azad University, North Tehran Branch, Iran

Introduction: Introduction: kombucha is a type of tea with a slightly sweet and slightly acidic taste. This drink is rich in acetic acids, gluconic and glucuronic acids and has a lower concentration of citric acid as well as a limited amount of ethanol and CO2. The synthesized acids lower the pH of kombucha tea and help to form its special sour taste. You can also use the coexistence of bacteria and yeasts to make fermented sweet black tea that is consumed around the world. This type of tea has a long history in China, Russia and Germany. This article examines the beneficial effects of kombucha, its chemicals and metabolites from fermentation depletion, as well as the properties of kombucha, with a particular focus on its probiotic potential. In addition, some contraindications to kombucha have been investigated in this study.

Methods: Material and methods: This drink is prepared by fermenting sweet tea with SCOBY. It tastes sour and sweet, and as a result of the fermentation process, carbon monoxide is produced. Kambucha is based on a variety of teas such as black tea, green tea or oolong. Recipes for making kambucha may be different, but usually by brewing black tea leaves with freshly boiled water, 50 to 150 grams per liter (5 to 15%) of sucrose, it is prepared for about 10 minutes and left in the dark for 7 to 10 days. If incubation continues for more than 10 days, the acidity may reach a level that is harmful to consumption. Next, the polysaccharide layer microbial colony is removed and the kombucha is ready to eat. The final product contains organic acids, vitamins, minerals.

Results: Results: The potential health impact has been exacerbated by the increase in kombucha. These include cholesterol and blood pressure levels, reduced release and improved liver, immune and gastrointestinal function. The beneficial effects of kombucha are attributed to the existence of biologically active components that acted synergistically. The bacteria in kombucha drink belong to the genus Acetobacter, Gluconobacter and Saccharomyces yeast, which together with glucuronic acid help protect health. kombucha is also considered a probiotic drink due to its diversity of naturally occurring microorganisms.

Conclusion: Discussion: Nowadays, by diversifying the production of kombucha, the amounts of its useful metabolites such as vitamins, organic acids and antimicrobial and antioxidant compounds can be optimized and used as a natural medicinal supplement.

Keywords: kombucha, Probiotic, Lactic bacteria, Acetic acid bacteria, Yeast

An overview of the role of stem cells in cancer therapy (Review)

Kimiya Shams,[1,*]

1. Department of Microbial Biotechnology, Faculty of Biological Science, North Tehran Branch, Islamic Azad University, Tehran, Iran.

Introduction: Cancer therapy has relied on various pharmacological and radiation-based interventions. There are numerous challenges in clinical cancer therapy. Often, the main cause is drug resistance. Stem cell therapy is a new and unique area of research in cancer therapy. Researching on the role of stem cells in cancer progression will lead to new therapies. It can target cancer cells at the first levels of pathogenesis. One of the other issues of chemotherapy is its lethal side effects, a focus on genetic and molecular therapies can provide the advancement of therapies of cancer with reducing side effects. Furthermore, the similarity between gene and surface antigen expression between embryonic stem cells and cancer cells represents that these cells can be used as an antitumor factor. Hence, here it is explored the role of stem cells in cancer therapy. It is observed that this stem cell vaccination could prevent the growth of tumors that were transplanted after the vaccination. Undifferentiated stem cells are powerful immunogens for generating an effective immune response against colon carcinoma, moreover, these cells induced strong tumor-specific cellular immune responses. Stem cells vaccination would increase lymphocytes and cytokines, so it leads to an antitumor effect. The tropism of mesenchymal stem cells to tumor sites makes them a suitable vector for therapeutic agent delivery to tumors and metastatic zones. Stem cells can be genetically modified to encode tumor suppressor genes, in addition, other techniques include stem cells loading with nanoparticles. Mesenchymal microvesicles are new drug delivery vectors. We summarized several studies in the fields of stem cells for immunization against tumors, using stem cells as drug carriers. Mesenchymal stem cells, which are undifferentiated cells with multifaceted potency and have the potential to regenerate themselves and differentiate into different cell lines, act as biological agents by regulating the immune system and releasing cytokines and chemokines into the inflammatory site. they do. These cells also play a very important role as carriers in delivering the drug to the original site of the tumor or the resulting metastasis. some research on immunization against tumors showed that mice immunized with embryonic cells could inhibit tumor growth. The unique capability of these cells is their versatility and long-term ability to self-renew. These properties enable them to repair and replace damaged tissue at the site of injury. In addition, these cells are inherently capable of migrating to areas of injury. As a result, they are discussed as a powerful tool in the treatment of chronic and cellular diseases Cancer, tissue engineering studies, and pharmaceutical applications

Methods: There is no methods part in review papers

Results: According to studies, mesenchymal stem cells in response to chemotactic signals released by pathogens or cells infected with these agents as well as abnormal cells can migrate to them. Consequently, these cells can be a good carrier for the transport of anticancer agents to the tumor site. Moreover, their therapeutic effects, which are related to their secretory factors, regulate innate and acquired immunity. In conclusion, clinical studies have shown that Mesenchymal stem cells are emerging as promising anti-cancer agents which have an enormous potential to be utilized to treat several different cancer types. MSC has inherent tumor-trophic migratory properties, which allows them to serve as vehicles for delivering effective, targeted therapy to isolated tumors and metastatic disease. MSC have been readily engineered to express anti-proliferative, pro-apoptotic agents that specifically target different cancer types.

Conclusion: Mesenchymal stem cells can regenerate and differentiate into different cell lines, and act as biological agents by regulating the immune system, and play a significant role as carriers in delivering the anticancer drugs to the original site of the tumor, and replace the damaged tissue.

Keywords: Mesenchymal stem cells, cancer therapy

An overview on Tissue Engineered Cartilage Products (Review)

Mohsen Safaei,[1] Zahra Abpeikar,[2,*]

1. Department of Medical Biotechnology, School of Advanced Technologies, Shahrekord University of Medical Sciences, Shahrekord, Iran
2. Department of Tissue Engineering and Applied Cell Sciences, School of Advanced Technologies, Shahrekord University of Medical Sciences, Shahrekord, Iran

Introduction: Articular cartilage has no blood vessels, nerves and lymph vessels accordingly, has a limited ability to repair itself after damage. Osteoarthritis is one of the most common joint diseases that result from the breakdown of articular cartilage and underlying bone and imposes high costs on countries' health care; thus, it is important to identify methods that stop or slow the progression of osteoarthritis. The Traditional strategies of surgery such as microfracture (MF), osteochondral autologous transplantation (OAT), osteochondral allograft transplantation (OCA), particulated articular cartilage implantation (PACI), and autologous chondrocyte implantation (ACI) have a limited ability for tissue repair and regeneration and have some limitations. Tissue engineering strategies as alternative approaches to current surgical procedures have raised new hopes for the repair and regeneration of articular cartilage.

Methods: This review information was accumulated from published papers, websites of companies and related patents.

Results: The tissue-engineered cartilage products can be divided into scaffold-free and scaffold-based approaches. Two products in the group of scaffold-free constructs include Chondrospheres®, also called ACT3D-CS or ARTHROCELL 3D®, and DeNovo® ET or RevaFlex™. Chondrospheres® are small spheroids formed by the proliferation of autologous chondrocytes and their associated ECM (Extra Cellular Matrix). RevaFlex™ is a disc composed of young allogeneic chondrocytes and their associated ECM. Studies have shown that young chondrocytes are better able to proliferate and secrete matrix than adult chondrocytes. Scaffold-based products can be divided into hydrogels and macroporous scaffolds. Cartipatch® and CaReS® are hydrogel scaffolds. Cartipatch® is an agarose-alginate hydrogel loaded with autologous chondrocytes. The CaReS® implant consists of type I collagen hydrogel containing autologous chondrocytes. The following can be mentioned from the category of macroporous scaffold: Matrix-induced Autologous Chondrocyte Implantation (MACI) is obtained from decellularized porcine peritoneal tissue loaded with expanded autologous chondrocytes. NeoCart® consists of a honeycomb bovine type I collagen scaffold loaded with expanded autologous chondrocytes. Thus, MACI and NeoCart® are both decellularized xenogeneic

grafts. Biocart™II is a fibrinogen/hyaluronic acid scaffold that is seeded with expanded autologous chondrocytes. NOVOCART®3D comprises a biphasic type I collagen scaffold loaded with autologous chondrocytes. Biocart™II and NOVOCART®3D scaffolds are fabricated using the freeze-dried technique. Hyalograft®C is a scaffold based on hyaluronic acid that is seeded with expanded autologous chondrocytes. Bioseed®-C comprises a polyglactin 910/poly-p-dioxanone fleece scaffold loaded with a fibrin solution and expanded autologous chondrocytes. Hyalograft® C and Bioseed®-C scaffolds both consist of woven and non-woven microfiber meshes. INSTRUCT is a poly (ethylene oxide-terephtalate)/poly (butylene terephtalate) (PEOT/PBT) scaffold loaded with bone marrow cells and primary autologous chondrocytes. Albeit, the details of this scaffold are unknown. A study explained the application of a Bioplotter device to fabricate a porous lattice construct with fibers approximately 170 µm in diameter, 200 µm pore size, and 56% of porosity. TruFit® and MaioRegen are among the cell-free scaffolds that have gone through the clinical trial phases and are now on the market. The TruFit® scaffold consists of a copolymer of polylactidecoglycolide, polyglycolide fibers, 10% calcium sulfate and surfactant. The MaioRegen scaffold is a three-layer biomimetic construct composed of collagen I and hydroxyapatite.

Conclusion: Cartilage tissue engineering is advancing with the identification of new scaffold fabrication techniques, the discovery of new stimuli, and improved surgical techniques that enable better regeneration of cartilage tissue. Comprehensive identification of current cartilage tissue engineering products provides a good basis for promotion the next generation of products.

Keywords: Cartilage, Tissue Engineering, Product, Osteoarthritis

An ultrapotent synthetic nanobody neutralizes SARS-CoV-2 by locking Spike into an inactive conformation (Review)

pollet betbenyamin,[1,*] Amir Ardalan Shokrollahi,[2]

1. institute of Higher Education Rab-Rashid
2. institute of Higher Education Rab-Rashid

Introduction: The major variant of concerns has shared mutations in severe acute respiratory SARS-CoV-2 spike proteins, mostly on the S1 unit, which resulted in a higher transmissibility rate and affect viral virulence and clinical outcome. The spike protein mutations and other non-structural protein mutations in the VOCs may lead to escape approved vaccinations. Nanobodies, single-domain fragments of camelid heavy-chain antibodies, have been developed to target a wide variety of viruses, frequently with the goal of using them as therapeutic agents. it has shown antiviral properties in various challenges with high affinity blocking SARS-CoV-2 spike interaction with ACE2 protein. A new strategy that allows the rapid and efficient engineering of mono- and multi-specific trivalent antibodies. reformatting nanobodies into multivalent constructs has been proposed to have a number of advantages for such antiviral purposes, including the potential to prevent conformational changes required for the virus to infect host cells.

Methods: In this review, we used online databases such as NCBI (PubMed), and google scholar. This research is the result of a survey of more than 50 articles, of which 26 articles were directly used in this study.

Results: SARS-CoV-2 is a positive-sense single-stranded RNA virus whose genome is of low stability thus is more prone to mutation accumulation, with approximately 9.8×10-4 annual substitutions/site. The S1 unit possesses the receptor-binding domain (RBD), which can directly bind to the ACE2 receptor and there is also the dominant target of neutralizing antibodies against SARS-CoV-2. S1 is thus considered a hotspot for mutations that may have high clinical relevance in terms of virulence, transmissibility, and host immune monomers that each avidly bind an RBD with an extreme combination of escape mutations. Nanobody multimerization has been shown to improve target affinity by avidity. In the case of Nb6 and mNb6, the structure-guided design of a multimeric construct that simultaneously engages all three RBDs yielded profound gains in potency. Furthermore, because RBDs must be in the upstate to engage with ACE2, conformational control of RBD accessibility serves as an added neutralization mechanism. Indeed, when mNb6-tri engages with Spike, it prevents ACE2 binding both by directly occluding the binding site and by locking the RBDs into an inactive conformation.

Conclusion: An outbreak of COVID-19 in Iran has spread throughout the country. Since the medical resources are limited, here, we aimed to identify the urgent issues that the world must consider to develop safe and effective preventions and therapeutics.

Keywords: Camelid, heavy-chain antibody, SARS-CoV-2,mNb6, diagnostic

An update review of globally reported SARS-CoV-2 vaccines in preclinical and clinical stages (Review)

Shirin Dashtbin,[1] Marzie Mahdizade Ari,[2] Hamid Motamedi,[3] Matin Fathollahi,[4] Hadi Hossainpour,[5] Ramin Abiri,[6,*]

1. Department of Microbiology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
2. Department of Microbiology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
3. Department of Microbiology, School of Medicine, Kermanshah University of Medical Sciences, Kermanshah, Iran
4. Department of Microbiology, School of Medicine, Kermanshah University of Medical Sciences, Kermanshah, Iran
5. Department of Microbiology, School of Medicine, Kermanshah University of Medical Sciences, Kermanshah, Iran
6. Fertility and Infertility Research Center, Health Technology Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran

Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent of the rapidly spreading pandemic COVID-19 in the world. As an effective therapeutic strategy is not introduced yet and the rapid genetic variations in the virus, there is an emerging necessity to design, evaluate and apply effective new vaccines. An acceptable vaccine must elicit both humoral and cellular immune responses, must have the least side effects and the storage and transport systems should be available and affordable for all countries. These vaccines can be classified into different types: inactivated vaccines, live-attenuated virus vaccines, subunit vaccines, virus-like particles (VLPs), nucleic acid-based vaccines (DNA and RNA) and recombinant vector-based vaccines (replicating and non-replicating viral vector).

Methods: Herein, we reviewed the different types of COVID-19 candidate vaccines that are currently being evaluated in preclinical and clinical trial phases along with advantages, disadvantages or adverse reactions, if any.

Results: According to the latest update of the WHO report on April 2nd, 2021, at least 85 vaccine candidates were being studied in clinical trial phases and 184 candidate vaccines were being evaluated in pre-clinical stages. In addition, studies have shown that other vaccines, including the Bacillus Calmette-Gu´erin (BCG) vaccine and the Plant-derived vaccine, may play a role in controlling pandemic COVID-19.

Conclusion: The recent pandemic, COVID-19 has resulted massive economic and social damages. Design and production of approved effective

vaccines against COVID-19 is of most importance. So far, eleven vaccines are licensed for larger-scale administration due to minimal side effects, stimulating strong immunity and neutralizing antibody responses, as well as high efficacy. These vaccines include: Oxford-AstraZeneca, Pfizer-BioNTech, Moderna, Sinopharm-Beijing, Gamaleya (Sputnik V), Sinovac, Sinopharm-Wuhan, Johnson& Johnson, Bharat Biotech (Covaxin), CanSino and Vector Institute (EpiVacCorona). The equitable distribution regardless of political issues and provision of adequate doses of these vaccines, especially for developing countries, may be the next challenge for COVID-19 vaccine. These vaccines are expected to reduce mortality rate significantly.

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

Analysis of long non-coding RNA expression among Iranian hemophilia A patients (Research Paper)

Elnaz Agi,[1] Ali Namvar,[2] Azam Bolhassani,[3,*]

1. Iranian Comprehensive Hemophilia Care Center, Tehran, Iran
2. Iranian Comprehensive Hemophilia Care Center, Tehran, Iran
3. Department of Hepatitis and AIDS, Pasteur Institute of Iran, Tehran, Iran

Introduction: LncRNAs are a group of non-coding RNAs with more than 200 nucleotides involved in transcriptional and post-transcriptional regulation of gene expression, and have potential in diagnosis, prevention and treatment of disorders like cancers. The goal of this study was to determine the relationship between the expression levels of specific lncRNAs and the incidence of hemophilia A in Iranian population.

Methods: Two lncRNAs (NONHSAT139215.2 and NONHSAT139219.2) were selected by the bioinformatics data for gene expression analysis using quantitative Real-time PCR based on their features. A 5 ml of whole blood in EDTA anti-coagulant tube was collected from 50 severe Hemophilia A male patients and 50 healthy male donors. Total RNA was extracted from peripheral blood using Favorgen Total RNA extraction Mini Kit. The cDNA was synthesized by reverse transcription method using Takara PrimeScript RT Reagent Kit. The expression of the selected lncRNAs was analyzed using qRT-PCR. The levels of lncRNAs were normalized by β2-microglobulin (B2M) expression levels as an internal control. The Pfaffl method was used to calculate relative gene expression, while accounting for differences in primer efficiency. The gene expression ratios for the lncRNAs were analyzed by the REST-2009 software.

Results: A comparison between the hemophilia and non-hemophilia groups demonstrated that the mean expression levels of two selected lncRNAs were significantly lower in hemophilia A samples compared to normal samples ($p < 0.05$).

Conclusion: Briefly, the low expression levels of NONHSAT139215.2 and NONHSAT139219.2 lncRNAs may be correlated with disease intensity in hemophilia A male patients.

Keywords: Hemophilia A; factor VIII; long non-coding RNAs, Real-time PCR

Analysis of Whole Exome Sequencing in a selected family with a Non-syndromic Glaucoma diseased Girl (Research Paper)

Parisima Ghafarian Zavarzadeh,[1,*] Morteza Jabbarpour Bonyadi,[2]

1. University of Tabriz
2. University of Tabriz

Introduction: Primary Congenital Glaucoma is frequently inherited as an autosomal recessive severe form of Glaucoma in infants and children, resulting from congenital anatomical defects in the trabecular meshwork. Predominantly Primary Congenital Glaucoma caused by pathogenic variants in the CYP1B1 or LTBP2 genes inherited in an autosomal recessive state and other candidate genes may have rule in the disease with their specific genetic inheritance pattern. We described a clinical, laboratory and genetically presentation of a pathogenic variant of CYP1B1 gene through a report of a case and a trio analysis of this candidate variant in the family with Sanger sequencing method and eventually completed our study with the secondary findings.

Methods: An 8-year-old girl referred to our glaucoma service for uncontrolled intraocular pressure (IOP). The case shows similar symptoms of Glaucoma at the early onset without any other set of medical signs and symptoms, clear that the unknown disease might be Primary Congenital Glaucoma in the form of non-syndromic. Whole Exome Sequencing data analysis of this case presented a candidate pathogenic Single Nucleotide Variant in CYP1B1 gene in homozygous state. Whereas this study terminated by Sanger sequencing method in both parents and the child to obtain the type of mutation and how it carried from parents to the offspring in case of inheritance.

Results: Although Clinvar has reported this candidate variant as a Conflicting interpretation of pathogenicity due to the different reports, further in-silico studies illustrate that the CYP1B1 variant c.G1103A (p.R368H) creates a nonsynonymous change which codes a different amino acid resulted in a disabling rule on the allosteric site of CYP1B1-related enzyme and classified as a pathogenic variant according to the American College of Medical Genetics and Genomics (ACMG) guidelines. Ultimately it revealed CYP1B1 (NM_000104) homozygous variant c.G1103A (p.R368H) as a related pathogenic variant to the distinct phenotype. According to the total findings the child was diagnosed with autosomal recessive Glaucoma3A because of the presence of the pathogenic variant (c.G1103A) in the CYP1B1 gene. Sanger sequence analysis method in the family revealed the pathogenic variant in a heterozygous state in her unaffected father but not her mother. However, our observations with the Integrative Genomics Viewer (IGV) tool

and Fastq file show details that GLC3A occurred due to the partial uniparental isodisomy between two RMDN2 and CYP1B1 genes at 2p.22 location.

Conclusion: The diagnosis was made based on Molecular findings of Whole Exome Sequencing data analysis. Therefore the clinical reports and bioinformatics findings were supporting the relation between the candidate pathogenic variant and the disease. However, it should not be forgotten that Primary Congenital Glaucoma is not peculiar to CYP1B1 gene. At last in this study, we presented the first case in Iran with Primary Congenital Glaucoma due to the partial uniparental isodisomy.

Keywords: CYP1B1,Partial uniparental isodisomy, PCG, Sanger sequencing, Whole Exome Sequencing.

Anti-cancer Effects of the Methanolic Extract of Frankincense on Brain Metastatic Breast Cancer Cells (Research Paper)

Mohammad Kamalabadi-Farahani,[1,*] Amir Atashi,[2] Maede Jafari,[3] Asma Asadi,[4]

1. Department of Tissue Engineering, School of Medicine, Shahroud University of Medical Sciences, Shahroud, Iran
2. Department of Medical Sciences, School of Paramedical, Shahroud University of Medical Sciences, Shahroud, Iran
3. Student Research Committee, School of Allied Medical Sciences, Shahroud University of Medical Sciences, Shahroud, Iran
4. Student Research Committee, School of Allied Medical Sciences, Shahroud University of Medical Sciences, Shahroud, Iran

Introduction: Background/Aim: Brain metastasis is a devastating complication in triple negative breast cancer (TNBC) patients. The anticancer properties of Frankincense was determined in many research, but on brain metastasis cancer cells, these effects have not been previously reported. This study aimed to evaluate these effects.

Methods: Materials and Methods: The methanolic extract of frankincense was prepared .After development of syngenic animal model of TNBC, primary breast cancer cells named 4T1T were isolated from tumor mass. Highly brain metastatic tumor cells named 4T1B were isolated and expanded from brain metastasis lesions of cancerous mice. The cytotoxic activity of Frankincense on 4T1B and 4T1T was assessed by MTT assays. Induction of apoptosis and antimetastatic effects of Frankincense was measured by annexin v- propidium iodide (pi) flow cytometric analysis and scratch test respectively.

Results: Results: The frankincense extract have potent apoptotic effects on 4T1B. Interestingly, 4T1B are more susceptible to apoptosis compared whit with 4T1T. Antimetastatic effects of extract was confirmed in 2D culture of these brain metastatic breast cancer cells.

Conclusion: Conclusion: This is the first report of the anticancer effects of frankincense extract on brain metastasis cancer cells. Compared to many anti-cancer drugs and compounds, which have very limited ability to fight on brain metastasis cancer cells, frankincense is a good candidate to combat these cells.

Keywords: Keywords: Triple Negative Breast Cancer, Brain Metastasis, Frankincense

Anti-telomerase and anti-proliferative effects of resveratrol, gallic acid, and kuromanin chloride in the PC3 prostate cancer cell line (Research Paper)

Reza Zarei,[1] Delaram Moghadam,[2] Fakhraddin Naghibalhossaini,[3,*]

1. Shiraz University of Medical Sciences
2. Shiraz University of Medical Sciences
3. Shiraz University of Medical Sciences

Introduction: Polyphenols, naturally occurring compounds in plants, exhibit a wide range of pharmaceutical properties (1). Resveratrol, gallic acid, and kuromanin chloride are dietary polyphenols belonging to the stilbenes, phenolic acids, and flavonoids classes, respectively (2-4). Studies during the past decades have shown the promising effect of these compounds in the prevention and treatment of different diseases such as Alzheimer's, diabetes, cancer, etc. (1). Telomerase is a ribonucleoprotein complex responsible for the de novo synthesis of the telomere. The elevated activity of telomerase was detected in approximately 85% of cancer cells (5). Several anticancer drugs exert their effects by inhibiting telomerase activity (6). Previous studies have suggested that some polyphenolic compounds may also have anti-telomerase activity against cancers (7). No study has compared the effect of three polyphenols of resveratrol, gallic acid, and kuromanin chloride, on telomerase activity in prostate cancer cells. The present study was designed to investigate the anti-proliferative and anti-telomerase effects of these polyphenols on the PC3 human prostate cancer cell line.

Methods: The human prostate cancer (PC3) cell line was obtained from the National Cell Bank of Iran (NCBI, Pasteur Institute, Tehran). The cells were cultured in RPMI-1640 medium supplemented with 10% fetal bovine serum (FBS) and 1% penicillin-streptomycin. PC3 cancer cells were treated with an increasing concentration (2.5, 5,10, 20, 40, 80) of resveratrol and gallic acid in a 96-well plate for 72h. The effect of compounds on cell proliferation was determined using the tetrazolium-based colorimetric assay (MTT assay). The cancer cells were then exposed to different concentrations (10, 20, and 40 µM) of polyphenols for 72h. At the end of the incubation period, the protein was extracted using an NP-40 lysis buffer. Protein concentration was measured by the Bradford assay, and telomerase activity was assessed by telomeric repeat amplification protocol (TRAP assay). Also, a trypan blue exclusion assay was performed to determine polyphenols' effect on cell viability.

Results: Compared to the control group, resveratrol, and gallic acid significantly reduced PC3 cell proliferation. The IC50 value of resveratrol and gallic acid for PC3 cells was 16.69 ±1.502 µM and 78.36 ±14.05 µM,

respectively. Kuromanin chloride had a negligible effect on the cell proliferation. The results of trypan blue exclusion assay indicated that all of these polyphenols reduce cell viability dose-dependently. Among the polyphenols, resveratrol had a substantial effect on reducing cell viability and proliferation. Compared to the control group, kuromanin chloride at all tested concentrations inhibited PC3 telomerase activity ($p< 0.01$). Gallic acid at 40 µM led to a significant reduction (40%) in telomerase activity ($p<0.01$). The telomerase activity in PC3 exhibited a reversed U-shaped response to different concentrations of resveratrol. Resveratrol at 20 µM significantly elevated telomerase activity by 34% ($p<0.01$), as compared to the non-treated control group. But, the change in the enzyme activity was not observed at other concentrations (10 and 40 µM).

Conclusion: The findings of the present study showed that all three polyphenols reduced cell proliferation and cell viability of PC3 cells. Resveratrol was the most effective polyphenol for inhibiting the proliferation of PC3 cancer cells. However, the change in telomerase activity was not correlated to the cell proliferation, which may be related to the other anticancer activity of these compounds. Previous studies have demonstrated that telomerase-dependent telomere shortening and consequently cell proliferation inhibition is dependent on several parameters such as initial telomere length and the required time for efficient telomere length shortening (8, 9). Our findings indicated that kuromanin chloride and gallic acid possess a considerable anti-telomerase effect. Further studies for evaluating the in vivo anti-telomerase activity of polyphenols against prostate cancer are needed.

Keywords: Gallic acid, Kuromanin chloride, Prostate Cancer, Resveratrol, Telomerase activity

Antibacterial activities and interactions of some essential oils against important human pathogenic bacteria: an in vitro study (Research Paper)

Mohsen Sheikhrezaee,[1] Mitra Mehrabani,[2] Alireza Golnaraghi,[3,*] Farzad Kobarfard,[4] Omid Hosseini,[5] Zahra Sheykhrezaee,[6]

1. Department of Traditional Medicine, Faculty of Persian Medicine, Kerman University of Medical Sciences
2. Department of Traditional Pharmacy, Faculty of Persian Medicine, Kerman University of Medical Sciences
3. Department of Biodiversity, BoomZista Institute
4. Department of Medicinal Chemistry, School of Pharmacy, Shahid Beheshti University of Medical Sciences
5. Department of Medicinal Chemistry, School of Pharmacy, Shahid Beheshti University of Medical Sciences
6. Department of Nature & Health, BoomZista Institute

Introduction: Emergence of antibiotic-resistant microbial strains and other issues related to antibiotic production/applications have revealed the fact that there are still challenges to overcome microbial epidemics and the treatment of infectious diseases. Persian medicine and its capacity could be considered as one of the choices to solve such issues. Although the words microbe or microbial diseases have not been mentioned in Persian medicine original books, the term Havaye Vabaee shares many similarities with contagious diseases. Particularly, a range of air-borne infectious diseases transmitted through inhalation fall into this category. Medicinal plants contain a variety of natural compounds with different benefits and properties. Applications of medicinal plants have been frequently described in Persian medicine. Several herbal elements, utilized in prevention and treatment of Havaye Vabaee diseases, are now classified into anti-oxidant, anti-microbial and bolstering immune system categories.

Methods: Antibacterial activities of essential oils (EOs) of some widely used herbal elements, including blacksamson echinacea, dill, chamomile, cinnamon, cumin, eucalyptus, lavender, myrtle, pennyroyal, peppermint, rosemary and thyme, whose antimicrobial effects are indirectly described in the old literature of traditional medicine as antiseptic agents and treatments of diseases caused by Havaye Vabaee, were investigated. Antibacterial activities of the EOs were evaluated against some important human pathogenic Gram-negative (Escherichia coli, Klebsiella pneumonia, Listeria monocytogenes and Pseudomonas aeruginosa) and Gram-positive (Staphylococcus aureus, Staph. epidermidis, and Streptococcus pyogenes) bacteria. To this end, minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC), and double-diffusion assay (DDA) tests

were utilized using a microdilution method. On the basis of MIC and DDA values, three EOs of cinnamon, eucalyptus and thyme with the highest antibacterial activities were then selected for checkerboard tests where antibacterial effects of double combinations of the EOs against E. coli and Staph. aureus were evaluated. The result of a checkerboard test was applied as input to calculate a fractional inhibitory concentration (FIC) index.

Results: Based on the results, the lowest MICs of the EOs were obtained for cinnamon followed by thyme and eucalyptus. These EOs also had the lowest values in MBC tests as compared with other EOs studied. The MIC and MBC values obtained for cinnamon were comparable with those obtained for the positive control used in this study (Gentamycin). While the reactions of the three Gram-positive bacteria to EOs were almost similar to each other, MIC and MBC values evaluated for the four Gram-negative bacteria were almost considerably different. DDA tests, in agreement with MIC and MBC assays, revealed the largest inhibition zones of the three EOs. Thyme followed by cinnamon showed the highest inhibition zones against different pathogenic bacteria. The values obtained were comparable with those measured for Gentamycin in most of EO-bacterium combinations. The FIC index values ranged from 1.0625 to 2 for Staph. aureus, and from 2 to 4 for E. coli. The lowest and the highest values were recorded for cinnamon-eucalyptus/Staph. aureus, and for cinnamon-thyme/E. coli and eucalyptus-thyme/E. coli combinations, respectively. The FIC index values were greater than 0.5 and less than 4, indicating “no interaction” between components of the combinations. The values calculated for cinnamon-thyme/E. coli and eucalyptus-thyme/E. coli combinations were 4, close to the cut-off value for antagonistic interactions.

Conclusion: The results indicated significant antibacterial properties of the three EOs. This characteristic can be attributed to their major chemical components and different antibacterial mechanisms involved. The differences observed in bacterial resistance and susceptibility to EOs are mainly due to the variation in bacterial cell membranes. Application of herbal elements is the main strategy in Persian medicine against different diseases, including those caused by Havaye Vabaee. Such combinations possibly affect a variety of biochemical and physiological processes in the human body and produce a plethora of interactions on the target microbes. Our study suggests that thyme oil must be used with caution as an antibacterial in combination with cinnamon or eucalyptus oils because antagonism may predominate; little is known about the mechanisms of antagonistic interaction. The results clearly indicate the necessity of investigation on the interactions of medicinal plants before formulating them as medicinal conoctions. We should warn patients to avoid the simultaneous use of herbal elements with chemical drugs without consulting with their physician, and try to change the general belief saying that use of herbal medicines is completely safe and healthy.

Keywords: Persian medicine, essential oils, combinations, antibacterial, antagonism

Antibacterial effect of lavender and rosemary essential oils nanoliposomes (Research Paper)

faezeh sarafraz,[1] Mohammad Javad Forouzani-Moghaddam,[2,*]

1. Msc of Food Microbiology, School of Paramedical, Iran University of Medical Sciences, Tehran, Iran
2. Msc of Food Microbiology, School of Paramedical, Iran University of Medical Sciences, Tehran, Iran

Introduction: After drying the plant in the shade, the essential oils of the sample were separated by water distillation using a Clevenger apparatus. The antibacterial effects of these plants were evaluated by disk diffusion method and preparation of successive dilutions. In order to control and standardize the method, antibiotic discs and standard bacterial strains were used.

Methods: Interactions showed that in dilutions of 1, 1 to 2 and 1 to 4, the inhibitory effect of lavender on five different bacteria together is more and more significant than rosemary.

Results: Comparison of the mean interactions of growth inhibition diameter between bacteria and dilutions of two plants showed that dilution 1 of essential oils has the greatest inhibitory effect on Proteus mirabilis. Also, comparing the different effects of lavender and rosemary essential oils on five different bacteria showed that dilution of 1, 1 to 2 and 1 to 4 of lavender essential oil had the greatest inhibitory effect on Proteus mirabilis compared to other bacteria and its inhibitory effect was more significant than rosemary. . Determination of MIC and MBC levels of lavender and rosemary essential oils showed that the bacteriostatic effect of essential oils on bacteria is similar to that of bacterium Throbacterium faecalis. However, the bactericidal effect of essential oils on all bacteria except Staphylococcus epidermidis is similar.

Conclusion: The results of disk diffusion method in comparison with gentamicin and streptomycin antibiotic disks showed the effect of this plant against the five-way growth studied.

Keywords: Antibacterial, lavender, rosemary, nanoliposome

Antibacterial Effects of Essential Oils of Montain Savory and Purple Coneflower on Staphylococcus aureus in vitro and Animal Model Study (Research Paper)

Nader Kazemi,[1,*] Kosar Abolfazli Zanjani,[2]

1. 1 Department of Biology, Nanobiotechnology Research Center, Zanjan Branch, Islamic Azad University, Zanjan, Iran
2. 2 Department of Microbiology, Nanobiotechnology Research Center, Zanjan Branch, Islamic Azad University, Zanjan, Iran

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.

Methods: In this study, essential oil was prepared from dried leaves of the Satureja montana and Echinacea angustifolia, 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 Satureja montana (30 mm), and the minimum of growth inhibition diameter is related to essential oil of Echinacea angustifolia (10 mm) at the highest concentration (400 mg/ml). In conditions of in vivo, spleen supernatant cultivation, the average number of bacteria for Satureja montana and Echinacea angustifolia 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 Satureja montana and

Echinacea angustifolia have the effective antibacterial activity against mentioned bacteria and can be useful to treatment of nosocomial infections.

Keywords: Antimicrobial, Echinacea angustifolia, Essential oil, Satureja montana, Staphylococcus aureus

Antibiotic Resistance in ESKAPE Pathogens (Review)

Roozbeh Yalfani,[1,*]

1. Department of Nursing, Faculty of Medical Sciences, Islamic Azad University,Varamin-Pishva branch, Tehran, Iran

Introduction: The ESKAPE pathogens (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species) are the leading cause of nosocomial infections throughout the world. Most of them are multidrug resistant isolates, which is one of the greatest challenges in clinical practice.

Methods: Multidrug resistance is amongst the top three threats to global public health and is usually caused by excessive drug usage or prescription, inappropriate use of antimicrobials, and substandard pharmaceuticals. Persistent use of antibiotics has provoked the emergence of multidrug resistant (MDR) and extensively drug resistant (XDR) bacteria, which render even the most effective drugs ineffective. Extended spectrum β-lactamase (ESBL) and carbapenemase producing Gram negative bacteria have emerged as an important therapeutic challenge.

Results: Development of novel therapeutics to treat drug resistant infections, especially those caused by ESKAPE pathogens is the need of the hour. Alternative therapies such as use of antibiotics in combination or with adjuvants, bacteriophages, antimicrobial peptides, nanoparticles, and photodynamic light therapy are widely reported.

Conclusion: Many reviews published till date describe these therapies with respect to the various agents used, their dosage details and mechanism of action against MDR pathogens but very few have focused specifically on ESKAPE.

Keywords: ESKAPE - pathogens - multidrug resistant

Antibiotics as anti-cancer agents (Review)

Ghazal arjmand kermani,[1,*] S Mahmoud A Najafi,[2]

1. University of Tehran
2. University of Tehran

Introduction: Introduction Human cancers are often associated with upregulation of proto-oncogenes and (or) downregulation of tumor suppressor genes. Investigation of the signal transduction pathways which participate in cancer development can lead to development of new drugs with both greater tumor cell specificity and improved efficacy. Recently it has been shown that some antibacterial agents have potential anti-cancer activities. Among many studies which support the anti-cancer properties of antibiotics, we provide several examples to highlight this very important issue.

Methods: We investigated Scopus and PubMed databases from 2010 through 2021 with keyword combination of “anti-cancer/anti-tumor” and “antibiotics”. We reached to 2,331 articles and based on the aim of the search, outcomes of interest included studies investigating signaling pathways affected by clinical antibiotics. Our data doesn’t include the combination of antibiotic therapy.

Results: Azithromycin, A Food and Drug Administration-approved antibiotic which has different anti-tumor effects including inhibition of tumor angiogenesis in lung cancer via blocking of vascular endothelial growth factor receptor 2 (VEGFR2)-mediated downstream signaling pathways. Fluoroquinolones are broad spectrum antibiotics which includes Ciprofloxacin as an example. Some of the Ciprofloxacin anti-tumor activities are: decreasing cell viability, inducing morphological changes plus S-phase cell cycle arrest, and induction of cell apoptosis through mitochondria dependent pathways in COLO829 melanoma cells. In addition, increasing in Bax levels and Bax/Bcl-2 ratio, and also a decrease in Bcl-2 concentrations in the human glioblastoma A-172 cell line are among other reported anti-cancer activities of Ciprofloxacin. Rapamycin-induced morphological changes of MCF-7 cells can lead to apoptosis. This macrolide fungicide has also been reported to prevent cell cycle progression of MCF-7 cells at the G0/G1 phase. Tigecycline which has a broad antibacterial spectrum against gram-positive and gram-negative pathogens, suppresses the activities of the mitochondrial-encoded proteins, Cox-1 and Cox-2 and therefore, results in downregulation of the mitochondrial electron transport respiratory chain and a reduction in oxygen consumption rate in Chronic myeloid leukemia (CML) cells. Tigecycline inhibits the proliferation of CML primary cells and cell lines including the drug-sensitive and drug-resistant cells and also induces autophagy by downregulating the PI3K-AKT-mTOR signaling pathway resulting in cell death by activation of

cytochrome-c/caspase-9/caspase-3 pathway. Also, Tigecycline induces autophagy in gastric cancer cells probably through suppression of mTOR/p70S6K phosphorylation. Monensin, an ionophoric antibiotic isolated from Streptomyces cinnamonensis, promotes apoptosis of melanoma cells via an increase in both expression of melanin granules and tyrosinase activity. This antibiotic also decreases clone and sphere formation of melanoma stem cells. The down-regulation of tyrosinase-related protein 2 (TRP-2) and Sox10 protein activity together with up-regulation of TRP1 have been linked to the increase in differentiation and the decrease in pluripotency of melanoma cells. This antibiotic shows anti-angiogenic activity by inhibiting capillary network formation, growth, migration and survival of endothelial cells. Furthermore, Monensin effectively targets tumor-associated endothelial cells and therefore, results in inhibition of glioblastoma angiogenesis and tumor growth.

Conclusion: The above examples plus many other laboratory and clinical results support that antibacterial drugs may have potential anti-cancer properties. These findings provide new directions toward searching novel anti-cancer drugs with more specificity and less side effects.

Keywords: Antibiotic, anti-tumor, cancer therapy

Antifungal susceptibility pattern and biofilm-related genes of Vaginal Candida species (Research Paper)

Dr.Faezeh Mohammadi,[1,*] Nima Hemmat,[2] Zahra Bajalan,[3]

1. Department of Medical Parasitology and Mycology School of Medicine Qazvin University of Medical Sciences
2. Cellular and Molecular Research Center, Research Institute for prevention of Non-Communicable Disease, Qazvin University of Medical Sciences
3. Social Determinants of Health Research Center, Qazvin University of Medical Sciences

Introduction: Vulvovaginal candidiasis caused by Candida species is a prevalent fungal infection among women. It is believed that the pathogenesis of Candida species is linked with the production of biofilm which is considered as a virulence factor for this organism. The aim of this study was molecular identification, antifungal susceptibility, biomass quantification of biofilm, and detection of virulence markers of Candida species.

Methods: We investigated the molecular identification of 70 vaginal isolates of Candida species, antifungal resistance to Amphotericin B, fluconazole, itraconazole, and voriconazole according to CLSI M27-A3 and S4, biofilm formation, and frequency analysis of biofilm-related ALS1, ALS3 and HWP1 genes.

Results: Our findings showed that the most common yeast isolated from vaginal discharge was C. albicans (67%) followed by the non albicans Candida species (33%). All C. albicans complex isolates were confirmed as C. albicans by HWP-PCR, and all isolates of C. glabrata complex revealed to be C. glabrata sensu stricto using multiplex PCR method. FLC resistance was observed in 23.4% of C. albicans and 7.7% of C. glabrata. Resistance rate to ITC was found in 10.6% of C. albicans. The frequency of ALS1, ALS3, and HWP1 genes among Candida species was (67.1%), (80%) and (81.4%), respectively. Biofilm formation was observed in 54.3% of Candida species and the highest frequency detected as virulence factor was for the ALS3 gene (97.3%) in biofilm forming species.

Conclusion: Our results showed the importance of molecular epidemiology studies, investigate of antifungal susceptibility profile, and understanding the role of biofilm-related virulence markers in the pathogenesis of Candida strains.

Keywords: Candida, Biofilms, Virulence genes, Vulvovaginitis. Antifungal susceptibility

Antioxidant Supplementation and Multiple sclerosis (Review)

Faeze qazanfaripoor,[1,*] Ali esnaashari,[2]

1.
2.

Introduction: Multiple sclerosis (MS) is a chronic, multifactorial disease of the central nervous system (CNS) characterized by inflammation and demyelination, which results in a heterogeneous array of symptoms including deleterious effects on motor, visual, sensory, and autonomic nervous system function. Research has demonstrated a link between MS and oxidative stress. Oxidative stress is a crucial factor in MS pathogenesis by ameliorating leukocyte migration, contributing to oligodendrocyte damage and axonal injury. Reactive oxygen species (ROS) and reactive nitrogen species (RNS) are created in CNS of MS patients mainly by activated macrophages and microglia structures responsible for demyelination and axons disruption. Therefore, increasing antioxidant levels to counter oxidative stress has been proposed as a potential treatment for MS.

Methods: A review literature search of eligible studies was conducted in PubMed database from 2015 to 2021 for studies evaluating the association between Antioxidant treatment, oxidative stress and multiple sclerosis using the following search strategy: ("oxidative stress" OR "RONS") AND ("multiple sclerosis" or "MS") AND (“antioxidant defence” or “antioxidant supplementation” as keywords. We included studies who analyzed malondialdehyde (MDA), total antioxidant capacity (TAC) and antioxidant enzymes [superoxide dismutase (SOD), and glutathione peroxidase (GPx)] activity and oxidative stress biomarkers.

Results: The results of our review article suggest that while reduction in oxidative stress markers (e.g. malondialdehyde (MDA), tumor necro- sis factor (TNF)-α, interleukin (IL)-4, IL-6, IL-1β, nitric oxide, and total oxidative stress levels) from antioxidant supplementation has been observed, these studies have demonstrated very limited effects on MS symptoms. One original study suggests that CoQ10 supplements at a dose of 500 mg/day can decrease oxidative stress and increase antioxidant enzyme activity in patients with relapsing-remitting MS. Another study reported decreasing the population and activation of inflammatory T helper cells in multiple sclerosis (MS) patients using vitamin A derivatives (retinoic acids).

Conclusion: The antioxidant activity can be considered as one of the main factors responsible for the neuroprotective effect of antioxidant supplementation. Larger and long-term follow-up studies would be necessary

to confirm neuroprotective effects of antioxidant supplementation in MS patients. Such investigation is required for better understanding of the potential of protective effects of antioxidants in cellular immunology of MS neurodegeneration. Not only would that increase our knowledge about the disease mechanisms but also could help to establish new goals for innovative treatment methods and provide real therapeutic benefits in MS.

Keywords: Antioxidant defenses, Oxidative stress, Supplementation, Multiple Sclerosis

Antioxidants Role in Diabetes Mellitus Treatment (Review)

Armaghan Vaezlari,[1,*]

1. Physiology research center, Medical university of Jondi Shapour Ahvaz

Introduction: Diabetes is a chronic metabolic disorder that continues to present as a major health problem worldwide highlighting the importance of continued research and the need for novel methods to both prevent and treat this pandemic. This disease is characterized by absolute or relative deficiencies in insulin secretion and/or insulin action and is associated with chronic hyperglycemia and disturbances of carbohydrate, lipid, and protein metabolism. Recent evidence suggests that oxidative stress may contribute to the pathogenesis of type 2 diabetes mellitus by increasing insulin resistance or impairing insulin secretion. This has prompted investigations in the use of antioxidants as a complementary therapeutic approach. In this review we briefly summarize oxidative mechanisms implicated in diabetic complications.

Methods: In order to find relevant studies to the research question, a literature search using PubMed (last ten years) was performed using the following terms “Diabetes, “Reactive oxygen species (ROS),” “Oxidative marker,” “Oxidative stress (OS),” “Antioxidant”, “vitamin E”, “vitamin C” individually or/and in various combinations to retrieve the relevant literatures. This search was limited to human clinical trials.

Results: Results from previous studies showed that antioxidants may inhibiting the formation of ROS or scavenge free radicals or increase the antioxidants defense enzyme capabilities. In a prospective cohort study, vitamin C intake was found to be significantly lower among incident cases of type 2 diabetic patients. In three prospective observational studies, serum α-tocopherol levels were associated with lower risk of diabetes mellitus. In another prospective study cohort of more than 4000 non-diabetic subjects over 23 years, vitamin E intake was significantly associated with a reduced risk of type 2 diabetes mellitus. However, some clinical studies have failed to show a significant diabetes-related increase in oxidative stress markers and the beneficial impacts of antioxidants on the diabetes complications.

Conclusion: Antioxidants such as N-acetylcysteine, vitamin C, and α-lipoic acid are effective in reducing diabetic complications, indicating that it may be beneficial either by ingestion of natural antioxidants or through dietary supplementation. Therefore, routine vitamin or mineral supplementation is not generally recommended and the safety and efficacy of antioxidant supplementation in any future treatment, remains to be established.

Keywords: Diabetes mellitus, Oxidative stress, Antioxidant.

Antiviral activity of Bacillus clausii probiotic strain and bacterial supernatant against herpes simplex virus type 1: in vitro study (Research Paper)

Mehdi Gholami Barzoki,[1,*] Somayeh Shatizadeh Malekshahi,[2] Mohammad Shayestehpour ,[3]

1. Department of Virology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran
2. Department of Virology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran
3. Department of Microbiology and Immunology, Faculty of Medicine, Kashan University of Medical Sciences, Kashan, Iran

Introduction: Herpes simplex virus-1 (HSV-1) is an enveloped double stranded DNA virus belonging to herpesviridae family. It can produce a wide spectrum of clinical disorders in skin, eye, central nervous system (CNS) and genital tract with multiple sequelae. There are several commercially available antivirals to treat lesions caused by HSV-1 including acyclovir, valacyclovir, penciclovir, and famciclovir. However, long-term treatment may lead to drug resistance ranging from 3.5 to 10% in the immunosuppressed patients and with a lower frequency in the immunocompetent individuals. Probiotics are defined as “live microorganisms which when administered in adequate amounts confer a health benefit on the host”. Currently, the use of probiotic and their metabolic products have attracted research attention and represents a promising approach for the prevention and treatment of viral infections. Bacillus clausii (B. clausii) is a spore-forming, aerobic probiotic bacterium which its antimicrobial and immunomodulatory properties have been described previously. The aim of the present study was to investigate for the first time the potential antiviral activity of B. clausii probiotic strain and bacterial supernatant against HSV-1 in a series of in vitro experiments.

Methods: To determine the amount of infectious HSV-1 particle we performed 50% tissue culture infective dose (TCID50) assay. To evaluate the possible cytotoxicity of the B. clausii and bacterial supernatant the survival ability of the vero cells was determined by dimethylthiazolyl-diphenyl tetrazolium bromide (MTT) assay. The experimental conditions designed as pre-treatment, pre-incubation, competition and post-treatment assays which was performed by B. clausii, bacterial supernatant and HSV-1 on Vero cells, separately. For antiviral experiments, the HSV-1 was used with a multiplicity of infection (MOI) of 0.1. Bacterial with 106 CFU/mL and bacterial supernatant at 1/64 dilution was used for all the experiments. Vero cells treated with HSV-1 served as control. DNA was extracted by using the AmpliSens® RIBO-prep nucleic acid extraction kit (Moscow, Russia) according to the manufacturer’s instruction. Real-time PCR analysis was performed using a FirePol®

EvaGreen® qPCR Mix (Solis BioDyne, Estonia) with ABI StepOnePlus™ instrument. Data related to real time PCR and TCID50 were analyzed by t-student test using GraphPad Prism version 6.0 and comparing each treatment with control. P value <0.05 was considered as statistically significant.

Results: The results of MTT assay indicated that by incubation of Vero cells with B. clausii at a concentration of 104, 105, and 106 CFU/mL more than 80% of cells were viable. Moreover, incubation of Vero cells with bacterial supernatant at a concentration of 1/32, 1/64, and 1/128 more than 80% of cells were viable. Then, the concentrations used to evaluate the antiviral activity was 106 CFU/mL of bacteria and 1/64 for bacterial supernatant in all subsequent assays. The HSV-1 titer in the absence of B. clausii (control) was 7.66 Log10 TCID50/mL. After incubation of B. clausii and HSV-1 into Vero cells under pre-treatment, pre-incubation, competition, and post-treatment assay, the titer of HSV-1 was estimated 4.08, 4.83, 5.33, and 7.08 Log10 TCID50/mL, respectively. HSV-1 titers in pre-treatment, pre-incubation, competition, and post-treatment assays decreased by about 3.6, 2.8, 2.3, and 0.6 Log10 TCID50/mL in comparison with control, respectively. After incubation of B. clausii supernatant and HSV-1 into Vero cells under pre-treatment, pre-incubation, competition, and post-treatment assay, the titer of HSV-1 was estimated 5.5, 6.08, 6.41 and 6.91 Log10 TCID50/mL, respectively. HSV-1 titers in pre-treatment, pre-incubation, competition, and post-treatment assays decreased by about 2.2, 1.6, 1.2, and 0.7 Log10 TCID50/mL in comparison with control, respectively. Using $2^{-\Delta\Delta C}$ method, the amount of HSV-1 genomic DNA in different experimental assays was compared with the control and the results were presented as fold change. The greatest reduction in viral DNA occurs when either B. clausii or bacterial supernatant was added to the cells before adding the virus (pre-treatment).

Conclusion: These results collectively suggest that probiotic strain B. clausii and its supernatant have promising inhibitory activity towards HSV-1 in vitro. The possible mechanisms of action are aggregation of B. clausii on the cell surface and prevention of viral entry in early infection steps and production of antiviral compounds. Hence, B. clausii may be considered as a novel inhibitor of HSV-1 infection with potential therapeutic or prophylactic benefits. More research is needed to explore its potential activity in animal model.

Keywords: Antiviral activity, Herpes simplex virus, Probiotic, Viral infection

Apoptosis and cancer (Review)

Yegane Zahiri,[1,*] Roghayeh Gholizadeh Doran Mahalleh,[2]

1. Medical student, member of Young and Elite Researchers Club of Islamic Azad University, Zahedan, Iran
2. Department of laboratory sciences, Zahedan branch, Islamic Azad university, Zahedan, Iran

Introduction: Escape from apoptosis is one of the six symptoms of cancer. Tumor cells produce many messages, such as a response to DNA damage or oncological activation, that naturally induce apoptosis. Most of the cells that acquire cancerous characteristics are killed by apoptosis through tumor suppression pathways. However, tumor cells that acquire the mutations needed to escape the apoptotic response survive and proliferate. Apoptosis causes more mutations to accumulate. This draws our attention to the differences between tumor cells and normal cells.

Methods: In this review study, Iran Medex, Scopus, Pubmed, Web of Science, Google Scholar, Magiran and SID databases were used.

Results: Compared to healthy cells, tumor cells receive messages that induce apoptosis (such as oxidative stress and oncogen activation), but are more limited in triggering an apoptotic response than healthy cells. Because the apoptotic pathway is often defective in tumor cells. Due to the exposure of cancer cells to different stresses between cancer cells and healthy cells, there is a fundamental difference in the status of caspase activation. In summary, apoptotic messages stimulate the processing of precapsases in healthy cells, while apoptotic messages in cancer cells activate the cessation of the inhibitory effect of IAP on processed caspases. If the apoptotic pathway is efficient, initiating an apoptotic response in a tumor cell is more specific than in a healthy cell.

Conclusion: Apoptosis is an important mechanism of tumor suppression. Caspases Aspartate proteases are major molecular actors in the process of apoptosis. Apoptosis is triggered by extracellular death messages or internal stimuli, which act through external and internal pathways, respectively. Escape from apoptosis is a hallmark of cancer cells.

Keywords: apoptosis, cancer, caspase, tumor cells

Application of Artificial intelligence in Covid-19 genome analysis: A review (Review)

Zohreh Javanmard,[1] Marzieh Esmaeili,[2,*]

1. Department of Health Information Technology, Ferdows School of Paramedical and Health, Birjand University of Medical Sciences, Birjand, Iran
2. Department of Health Information Management, School of Allied Medical Sciences, Tehran University of Medical Sciences, Tehran, Iran

Introduction: Until now, many studies were done to more recognition of coronavirus (Covid-19) and its characteristics. Analysis of the Covid-19 genome is one of the noticeable subjects in this scope. Evaluation of the Covid-19 genome sequencing can provide valuable information about the origin of the virus, its behavior, mutations, and effective therapeutic methods. The use of Artificial Intelligence (AI) techniques is an important method to analyze the Covid-19 genome and extract its features. Deep learning, machine learning, digital signal processing, and deep neural network, are some examples of AI techniques that can be used for the investigation of Covid-19 genome. Therefore, the present study aims to investigate the AI techniques used in Covid-19 genome analysis.

Methods: In this review, a comprehensive search was done in August 2021 through PubMed with the keywords of “Covid-19”, “Genome” and “Artificial Intelligence” alongside their synonyms in the titles and abstracts of the papers published from 2019 to 2021. The original studies which were related to Covid-19 genome analysis by AI techniques were selected; and non-English papers were left out.

Results: The search resulted in 644 papers, among which 21 papers addressing Covid-19 genome analysis by AI techniques were selected based on their titles and abstracts. About 57% (12 of 21) of the studies, used AI techniques to extract hidden patterns, frequent patterns and characteristics of Covid-19 genome sequences. 71% (15 of 21) of the studies, using AI methods and genome information, made predictions about virus mutations, outcomes severity, localization/residency, reservoir host, host proteins that bind to the Covid-19 RNA genome, subsequent structures of virus proteins, genomic similarities of Covid-19 and other viruses, and subsequent sequences of the virus genome. 31% (8 of 21) of the studies, analyzed and identified virus mutations, based on genome sequence information and AI techniques. In most studies, NCBI GenBank (11 of 21) and GISAID Database (6 of 21) have been used to gather genome sequences. Long Short Term Memory (LSTM), random forest classifiers and decision trees were the most widely used AI techniques in the reviewed studies.

Conclusion: The application of artificial intelligence in discovering the genetic features of Covid-19 is very wide, applications like classification and discrimination of Covid-19 disease from similar diseases, extract hidden patterns, investigate the origin of the virus, and predicting the subsequent Covid-19 structures. Therefore, the use of AI alongside genetic is so valuable to the management and control of coronavirus pandemic, as well as the development of vaccines and therapeutic methods.

Keywords: Artificial intelligence, Covid-19, Genome, Mutation, Vaccines

Application of Bone Marrow Stromal Cells in Chemotherapy-induced Premature Ovarian Failure (Review)

Fatemeh Mohebi,[1,*] Mina Soleimani,[2] Hanane Hamidi,[3]

1. Molecular Medicine Research Center, Hormozgan Health Institute, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
2. Iran University of Medical Sciences, Tehran, Iran
3. Khalkhal University of Medical Science, Khalkhal, Iran

Introduction: Introduction: Female infertility is a worldwide therapeutic condition that can be caused by various reproductive system-related diseases, including premature ovarian failure (POF) and polycystic ovary syndrome (PCOS). Even though chemotherapy drugs can reduce the tumor cell's growth, they can also cause premature ovarian failure and consequently female infertility. It affects the quality of both the physical and mental health of patients. As a possible cell-based treatment, Mesenchymal stem cells (MSCs) have obtained rising attention. Bone marrow-derived mesenchymal stem cells (BMSCs) feature advantages such as self-replication, multidirectional differentiation, convenient source, ability to avoid immune rejection, and lack of ethical issues. Moreover, BMSCs have extensive utilization potential in the regenerative medicine, including reproductive dysfunction.

Methods: Methods: The data were collected using 15 articles in Pub Med and Science Direct, between 2014 and 2021 by using keywords BMSC, POF, Mesenchymal stem cells.

Results: Results: 4 pieces of research have shown advantageous effects of BMSCs therapy in a chemotherapy-induced ovarian failure in animal models. Especially the results demonstrated that bone marrow stromal cells can restore ovarian structure and functions. After all, the beneficial effects of BMSC treatment in clinical trials is not adequately to certify that most POF patients will repair their ovarian reserve.

Conclusion: Conclusion: The purpose of the current study was to determine the beneficial effects of bone marrow stromal cells on ovarian dysfunctions. BMSCs are a good candidate for transplantation in ovarian dysfunction because of their low immunogenicity, also they can be obtained easily and amplified in large quantities in vitro but BMSCs are not widely applied in clinical therapy.

Keywords: Keywords: BMSC, POF, Mesenchymal stem cells

ApplyingGenomics technologyforEarly Detection of Reproductive Tract concer (Review)

Kian Nouri,[1,*]

1. Hazrat Mohammad High School

Introduction: Genomics is a new science whichstudies allgenes in an organism, structure ofgenes, and the interaction of geneswith each other and the organismenvironment. Adrances in molecular bilology In recent decadehas helped researchers flgure out the complexgenetic changes, transcription, translation of human cancers.These molecular changes are the basis of efficient and growing techniques of cancer detection, which require microscopic is one of these new diagnostic technologies discovered in recent years for facilitating the genome imestigation and proteome of cancerous cells.Review studies of structural, comparative and functicnal genomics prepares the ground for a detailed and better image of genome structure and performance . Today, more efficient methods are avaible to help researchers investigate and confirm, mRNA and protein transcript.Genomics is applicable for finding new drugs, new genes, non-coding DNA, gene projects, identification of repetitive sequence, and mutations.

Methods: Numerous technologies have been used to detect cancer markers, classify them, and apply them to clinical applications. Laser microscopic cutting is one of the first group of these technologies. This method makes it possible to accurately separate tumor cells, stromal cells, and healthy cells from a biopsy specimen. Optimal examination of isolated microscopic specimens allows accurate separation of events within and between each of these tissue subunits. The use of these methods in patient specimens has made it possible to explain genomic changes, gene expression events and gene expression differences, activation and marking of different proteins in tumor specimens. Non-cancerous occurs in the relevant groups. The development and application of these technologies in clinical trials has promised advances in early detection of cancer, prevention, and specific tumor treatments. By increasing researchers' understanding of specific changes in the expression of genes and protein signaling pathways, it is possible to change the basis of treatment from pathohistopathology to specific treatment of deregulated molecules due to host tumor interaction. Of course, it can not be said that these methods are a complete replacement for conventional methods in the treatment of diseases. Genomic and proteomic advances in guiding researchers will help select the best treatment for each patient. All genomics techniques are involved in identifying unknown targets in the tumor genome and proteome. Identifying specific changes in tumor DNA, RNA, and proteins requires knowing what is happening in and around the tumor. In the past, researchers' ability to pinpoint the exact location of these

changes was impaired due to the weakness in isolating specific cell types from the pathology specimen. Cell-scraping, purification with a hybrid column, culture of immortal cells in the culture medium of cell culture and manual dissection of tissues. All of these methods are used, each with its own advantages and disadvantages. Although these techniques have led researchers to develop pure cell lines to evaluate intracellular currents, some of the information that determines the phenotype of a particular tumor type. Will be lost; For example, the environment around a cancerous tumor includes not only malignant epithelial components, but also the surrounding stroma and surrounding healthy tissue. These microscopic components, using receptors, cell junctions, intracellular and intracellular signal molecules, allow tumor cells to communicate with their surroundings and also play an active role in controlling or promoting them. Removal of some of these components for culturing cells in vitro disrupts cell-cell and cell-matrix interactions, which may affect tumor behavior, resulting in a misconception of the structure and physiology of the tumor in the living cell medium. . Using genomics technology, it is possible to evaluate thousands of genes simultaneously by amplifying RNA using fluorescent signals and then applying these transcripts to array plates that contain large amounts of oligonucleotides or cDNAs. The presence of a fluorescence marker indicates the presence and size of a pure cDNA transcript in the study population. Differences in gene expression are recorded and gene expression patterns are calculated using several microarrays simultaneously and by comparative bioinformatics software. The information obtained from the study of the tumor genome and its transcripts leads to advances in the discovery of new genes and cancer detection methods. Tissue microarrays are one of the new technologies that have recently become available in recent years to facilitate the study of the genome and proteome of cancer cells. Tissue microarrays are essentially useful tools for the rapid and convenient analysis of a large number of paraffin-coated tissues belonging to a variety of tumors. The application of this technology allows the use of the same probe and brings the standard of interpretation of the results closer to the standard. This tool facilitates the analysis of the expression of several genes and their amplification in a tumor or a region of the tumor by a standard method. Microarray findings in breast cancer research address two main issues; First, individual tumors originating from one organ may be classified into different groups based on the pattern of gene expression, independent of stage and stage of progression. Second, biological findings from such classifications can be used for diagnosis. Studies have shown that microarray technology makes it possible to study tumor behavior in living tissue and to evaluate the method of diagnosis and drug resistance. Examining the expression of thousands of genes shows that there are many differences between tumors that originate from a single organ. Although DNA microarray technology in gene expression analysis has not made progress in the clinical treatment of breast cancer patients, it does

provide information on the pathways and molecular mechanisms in biological activity.

Results: Low molecular weight proteins are present in the serum sample. Then they have done it with powerful and new bioinformatics tools to classify cancer and non-cancer in the relevant groups. In recent years, dramatic advances have been made in various microscopic techniques such as light microscopy, immunohistochemistry, and methods based on the use of antibodies to diagnose and test different types of cancer. These kinds of technological advances have been in the early detection and treatment of a number of cancers, such as malignant cervical cancer. In machine cancers, such as molecular techniques such as PCR and hybridization, products have been developed to find subtypes of human papillomavirus (HPR) dangerous in cervical cancer. Be. Ornstein et al. Tested the effect of the tumor environment on its proteome and isolated the prostate tumor from prostate specimens using LCM optillium and stromaline. Recent information on protein obtained by two-dimensional electrophoresis of cell extract samples Isolated, isolated whole extract, and immortalized cell lines belonging to the same patient were performed together. Further comparisons were made using uterine data from two existing prostate cancer cell lines. Their findings are very important. First, the stromal and epithelial compounds of the tumor were located in half of the common protein. Second, the proteins that expressed differently in healthy and malignant tissue were located exclusively in the epithelial region. Third, quality microscopic secretion. They did not alter the protein. They also found that protein properties were tested in the living and environmental environment, and that only 25% of the total protein and other key LCMs play a role in specific genomic features in helping me compare DNA, RNA, and protein I walls. It reveals its texture and function in healthy and neoplastic tissues.

Conclusion: Due to the increasing cost of sequencing and genome testing, increasing the efficiency of existing methods, advances in chemistry, and the arrival of new generations of sequencing, patients who come to medical facilities are likely to bring their gene sequencing with them in the future. However, this is not a overnight revolutionary trend, as phenotype predictions based on genotypic findings are still severely constrained, and there is still a long way to go before genomic technologies of good quality and low cost emerge. Current and emerging technologies in reproductive biology, including assisted reproductive technology and animal cloning, discuss the impact of genomic biology. The discussion focuses on the glands associated with the establishment and maintenance of pregnancy, placental development, lactation, and neonatal survival. Various aspects of uterine biology, including neonatal development and function in adult females, are discussed with respect to reproductive efficiency. It is clear that combining strategies for using conventional animal models to study the reproductive system with new

genomic technologies provides exceptional opportunities in discovery research involving data integration and the use of functional genomics for the benefit of animal husbandry and the medical community. New emerging biotechnology and adaptive and genomic methods will greatly enhance our understanding of genes that are critical to the development of the reproductive system and key events at each stage of the reproductive cycle in both men and women.

Keywords: Genomics, Early Detection, Cancer, Reproductive organ,Dvary,Endometrium

Artificial intelligence in the service of genetics: applications and challenges (Review)

Shiva Pouyanfar,[1,*] Nafiseh Soudi,[2]

1. Student Research Committee, Alborz University of Medical Sciences, Karaj, Iran
2. Department of Laboratory Sciences, Tabriz Faculty of Paramedicine, Tabriz University of Medical Sciences, Tabriz, Iran

Introduction: Advances in technology in recent years have had many and varied effects on medical science. Artificial intelligence is a rapidly growing technology that, in addition to its various roles in everyday human life, also plays an important role in different fields of science (including medicine). On the other hand, one of the fields of medicine that has always been developing rapidly is the field of genetics, which is closely related to technology. The combination of artificial intelligence and genetics is a topic that can be very challenging and regarded as an applied field of study.

Methods: by studying the researches conducted in this field in recent years, we gained an overview of the subject.

Results: Artificial intelligence has wide applications in medicine; including collecting patient information and suggesting possible treatment methods, classifying patient information in statistical studies, facilitation of communication between autistic children and their therapist, diagnosing some fetal abnormalities, assessing fetal viability based on fetal imaging analysis, diagnosing diabetic retinopathy through retinal imaging analysis and classifying patients based on the diagnosis, etc. Particularly in the field of genetics, artificial intelligence and its various forms (machine learning, deep learning, natural language processing, etc.) are used in information gathering, risk assessment, genome sequencing, pedigree drawing, designing algorithms for specific genetic diagnostic testing, polygenic risk scores for complex conditions, gene-editing CRISPR, literature mining, next-generation sequencing (NGS), variant calling, genome annotation and variant classification, genotype-to-phenotype prediction, phenotype-to-genotype mapping, etc. Despite the widespread use of artificial intelligence in medicine and genetics, there are limitations and challenges, including the need for large datasets, the black box nature, regulatory issues, privacy, human resistance, data and machine bias, and so on. Of course, the constant challenge in the field of artificial intelligence has been the fear of humans being replaced by machines, which still exists.

Conclusion: Artificial intelligence is an evolving technology that can reduce the extra workload of geneticists by performing certain tasks, and by saving more of their time and energy, can play an important role in providing better and more accurate services.

Keywords: artificial intelligence, genetics, next-generation sequencing

Assessing the ethical aspect of genome editing considering CRISPR technique (Review)

Mohammad Reza Dabbagh ,[1,*] Seyed Sobhan Bahreiny,[2]

1. Department of Biology, University of Qom, Qom, IRAN
2. Department of Biology, University of Qom, Qom, IRAN

Introduction: After achieving the genome editing ability, huge prospects were created for curing genetic diseases and lots of the defects corresponding to other previous techniques were resolved by CRISPR-Cas9 editing system and there was actually a revolution in this area but, on the other hand some concerns were propounded about the ethical challenges this technology can bring with itself such as genome editing at the embryonic level, genetic discrimination, unequal accession and …. As a result, in corresponding conventions and international statements, there is always an assertion on applying the required conditions and protocols about the matter of genome editing.

Methods: In this review article in order to assess the ethical aspect of genome editing, first the declarations and universal statements related to genome editing like act compiled in Oviedo convention, universal declaration of human genome and also the statements of clinical experiments such as Helsinki statement and … are used and also the challenges of genome editing is evaluated with respect to the compiled rules for it. Then by examining the advantages and disadvantages of genome editing and also the background and result of the edits which are done so far at the genomic level, it was tried to gather different opinions about the genome editing and ethical issues related to that.

Results: In all legal texts, reports, declarations and statements which are published regard to venerating the subjects under experiments, respecting the rights of subjects and the principle of self-determination and profitability of individuals is reassured. Same rules and protocols and sometimes more necessitated ones are stated according to genome editing. However, having technical approvals of CRISPR technique and applying the compiled protocols related to genome editing and also close surveillance on enforcing the stated rules can lead to the effective treatment of genetic disorders.

Conclusion: The matter of genome editing although is in the beginning of its road to success but needs lots of attention regard to ethical issues and preserving the involved individuals' rights and therefore along with the scientific advanced in this field, special attention should be paid to updating

the ethical protocols, specially to the genome editing at the embryonic level, so that the best decision can be made according to the situation.

Keywords: Genome editing – CRISPR – Gene – Bioethics

Assessment of different doses of nickel chloride on RBC, Hemoglobin and hematocrit in female Wistar rats (Research Paper)

Zahra Azmoun,[1] Seyed Mohammad Hosseini,[2,*] Sohrab Kazemi,[3]

1. Department of Pathology, Islamic Azad University, Babol Branch, Babol, Iran
2. Department of Pathology, Islamic Azad University, Babol Branch, Babol, Iran
3. Cellular and Molecular biology research centre, health research institute, Babol University of medical sciences

Introduction: Nickel is one of the main heavy metals in the environment, which is present in the crust and core of the Earth. Although nickel is essential to many microorganisms and plants, if humans get exposed to a high amount of nickel, they might reveal different anomalies. As extensive quantities of studies have been implemented during recent years, numerous teratogenicity, Hemotoxic, and allergies that have been reported are attributed to nickel effects which people can be exposed through either gastrointestinal tract or inhalation. The current work was done to determine the impacts of sub-acute exposure with three doses of nickel chloride on some hematologic criteria in adult female Wistar rats.

Methods: 32 Wistar rats were used and distributed randomly into 4 groups, group one was considered as control which was administered 0.5 ccs of distilled water by intraparietal injection, and groups two three, and four obtained Nickel by doses of 10, 15, and 25 mg/kg in order by intraperitoneal injection.

Results: Our findings exhibited that nickel chloride administration causes moderate alteration of complete blood count values in Wistar rats treated with 10 and 15 mg/kg dose while marked changes were seen in rats treated with 25mg/kg dose. Moreover, According to the levels of HCT and HGB of the 4th group, which are the lowest among all the groups, the dose 25 mg/kg indicated as the most toxic dose in this investigation.

Conclusion: To sum up, we can conclude that these side effects are consequences of free radicals due to Nickel treatments and According to low levels of RBC, HCT, and HGB it ought to be reckoned that nickel has negative impacts on human and animal health and toxicity effect of nickel could be considered as one of them.

Keywords: HCT, HGB, RBC, Hematology, Wistar Rat

Association between Coronary Artery Disease and rs10757278 and rs1333049 Polymorphisms in 9p21 Locus in Iran (Research Paper)

Farbod Yaghoubi Hariri,[1] Iman Salahshourifar,[2,*] Shohreh Zare Karizi,[3]

1. Department of biology Science and Research Branch Islamic Azad University
2. Department of biology Science and Research Branch Islamic Azad University
3. Department of Genetics and Biotechnology School of Biological Science Varamin-Pishva Branch,

Introduction: Coronary artery disease is one of the most common causes of death worldwide. An estimated 3.8 million men and 3.4 million women die each year from CAD .The prevalence of CAD in the Iranian population is responsible for almost 50 percent of all deaths each year.Hence, detecting high-risk patients is important. Fortunately, CAD risk can be predicted based on family history, the level of adipose cells, blood pressure, and smoking status. Of these, family history is most important. Recent studies have identified a major role for genetic factors. Hence, more than 100 genes are effective in the emergence of CAD by producing atherosclerosis plaques. Correlation studies have identified several genetic variants that are effective in the emergence of multifactorial diseases such as CAD. One of the loci identified as a hotspot for CAD is 9p21.3 in various populations . The 9p21.3 locus has been found to be associated with CAD in Caucasian, Italian, American, Spanish, Southeast Asian, Indian, and Pakistani populations . No protein-coding gene has been thus far detected in the 9p21.3 locus, however this 58 kb region harbors the CDKN2B-AS (inhibitor 2B antisense RNA cyclin-dependent kinase) gene, which encodes an antisense noncoding RNA . CDKN2B-AS is located near the CDK inhibitor genes CDKN2A (cyclin dependent kinase inhibitor 2A), and CDKN2B, which both inhibit CDK4 and regulate cell growth. It has been reported that the rs1333049 variant in the INK4 locus (ANRIL), near the cell cycle regulating genes, plays a role in CAD risk. In addition, it has been documented that the rs10757278 variant is located in one of the identified enhancers in the 9p21 locus. The risk allele of this variant disrupts the binding site of STAT1 protein and alters the cellular response to inflammation, angiogenesis, and atherogenesis .

Methods: Two hundred blood samples from Iranian CAD patients and normal healthy controls were collected. CAD and the 9p21 locus variants rs1333049 and rs10757278 were analyzed for potential associations. Three ml of peripheral blood were collected from each subject and stored in EDTA-containing tubes. Genomic DNA was extracted from peripheral blood cells according to the manufacturer's instructions. Specific tetra-ARMS PCR primers were designed for genotyping of each variant using Primer1 software

. PCR products were then electrophoresed on 3% agarose gels and stained with green viewer dye. To optimize the tetra-ARMS PCR, each genotype of both variants for a few samples was directly sequenced. Sequences were analyzed using BioEdit software .For genotyping, in each PCR run, three control samples with known genotypes were amplified alongside the unknown samples. The FAMHAP software program was used for Hardy-Weinberg testing, genotype and allele frequency calculation, and haplotype/diplotype analysis.

Results: The PCR product for each variant was visualized using agarose gel electrophoresis. Sample genotypes were determined by amplifying them alongside control samples of known genotype.Neither variant was in Hardy-Weinberg equilibrium in either the case or control groups. Allele and genotype analyses found no significant association between either variant and CAD risk .Haplotypes differed significantly between then the two groups (X2= 8.7836, df= 3, p= 0.0323), with the CG haplotype more frequent in the control than in the CAD group, indicating a protective role for this haplotype against CAD.In diplotype analysis which is the combination of haplotypes on each chromosome, combination of CA haplotype of rs1333049-rs10757278 variants and GA haplotypes of rs1333049-rs10757278 variants showed increased the risk of CAD (CI= 1.13-5.69, OR= 2.53). While in contrast, combination of CA haplotype of rs1333049-rs10757278 variants and CA haplotypes of rs1333049-rs10757278 variants showed a protective role (CI= 0.13-1.14, OR= 0.386)

Conclusion: In this study, the rs10757278 and rs1333049 polymorphisms in the 9p21 locus were analyzed for their association with CAD. No significant associations were found between the two polymorphic genotypes and CAD risk (p> 0.05).The above findings can be explained by different allelic distributions in various populations or low frequencies of some alleles in the target population. Additionally, a variety of ethnic groups live in Iran, each of which can have a specific allelic frequency, affecting the results of such studies. In addition, CAD is a multifactorial disease influenced by environmental factors. Ultimately, SNPs create a genetic potential for an individual, the expression of which depends on one’s genetic background, interactions between other genes, and the environment. Future studies are recommended.

Keywords: Coronary artery disease (CAD), Polymorphism, rs1333049, rs10757278, 9p21

Association between Hepatitis B Virus (HBV) infection and variety of cancers, including liver cancer (Review)

Mahsa Rahnein,[1] Azin Sarhadi ,[2] Shaghayegh Yazdani,[3,*]

1. BS student in Microbiology,Faculty of Advanced Science & Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran
2. BS student in Microbiology,Faculty of Advanced Science & Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran
3. Department of Microbiology, Faculty of Advanced Science & Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

Introduction: HBV infections can be acute or chronic. Acute liver infection is jaundice with elevated serum aminotransferase. Cancer caused by liver cirrhosis causes HCC (hepatocellular carcinoma). Hepatitis B contains a surface antigen called HBsAg, which can cause a chronic infection if it stays in a person's blood or serum for a long time (six months or more). The routes of transmission are primarily from mother to child through the placenta, sexual path and infected needles. The chronic form of HBV has worse results than the acute form. The liver plays an important role in maintaining adequate glucose levels, transporting nutrients, and filtering toxins so that this infection can pose a serious risk. Joint infection of the liver with HCV causes fibrosis and cirrhosis and leads to cancer. By producing a circular DNA-shaped plasmid, the virus optimizes its life cycle for long-term survival in liver tissue.

Methods: Several studies have been conducted to investigate the association between HBV infection and various cancers, including liver cancer. One of these studies was conducted in China between 2004 and 2008to determine the association between this infection and all cancer types. In this study, a dipstick test was used (a test to detect abnormalities that contain chemical strips that change color if there is a disease); this test was used to detect hepatitis B surface antigen (HBsAg). Blood tests for people with HBV are generally used to diagnose this infection. Laboratory diagnosis of HBV also focuses on the detection of its surface antigen. Polymerase chain reaction (PCR) is a highly sensitive technique for the detection of hepatitis B virus DNA in serum, liver tissue and mononuclear blood cells. Therefore PCR is another method of diagnosing HBV, especially in chronic HBV and people with HBsAg positive and for follow-up HBV infections in liver transplantation programs.

Results: Studies in China have shown that participants who were HBsAg positive had a higher risk of hepatocellular carcinoma (HCC), stomach cancer, colorectal cancer, oral cancer, pancreatic cancer and lymphoma when compared with participants who were HBsAg negative. The persistence of HBsAg is the principal marker of risk for developing chronic liver disease and liver cancer later in life.

Conclusion: This study found that HBV infection was also associated with the risk of nonliver cancer, especially digestive system cancers.

Keywords: HBV infection , HCC , cirrhosis , chronic.

Association between thrombophilia gene polymorphisms and recurrent pregnancy loss risk in the Iranian population (Research Paper)

samaneh heidarzadeh,[1] Razieh Bigdeli ,[2] Vahid Asgary,[3,*]

1. Research and Development Laboratory, Javid Biotechnology Institute, Tehran, Iran
2. Research and Development Laboratory, Javid Biotechnology Institute, Tehran, Iran
3. Research and Development Laboratory, Javid Biotechnology Institute, Tehran, Iran

Introduction: Miscarriage is the most common complication in pregnancy. The pathophysiology of recurrent pregnancy loss (RPL) is a complex problem and poorly understood. Many believe that RPL is influenced by different factors such as abnormalities in chromosomes, anatomic, endocrine, immune defects, and also infections (Garcia-Enguidanos et al. 2002; Ford and Schust 2009; Jaleh et al. 2011). Thrombophilia is one of the major cause of RPL (Buchholz and Thaler 2003; Di Micco et al. 2007; JeddiTehrani et al. 2010). This compelling fact that patients who have inherited thrombophilic abnormalities show higher risks of RPL, has encouraged researchers to investigate patients with RPL, and look for its relation to thrombophilic polymorphism frequencies (Coulam et al. 2006) . During pregnancy, changes in the body systems of mother resulting in changes in the homeostasis results in the hypercoagulable state of pregnancy. As a result the risk of thrombophilia becomes greater which can reflect many genetic factors such as polymorphisms which later affect the coagulation system and folate metabolism pathway (Goodman et al. 2006). Genetic researchers worldwide are trying to look for RPL candidate genes and have performed various experiments on many different genetic variants. The main focus of these experiments is on the mutations that cause thrombophilia and it is thought that it is inherited maternally. But, it is still controversial whether thrombophilic gene mutations are an important factor in RPL (Brenner 1999; Blanco-Molina et al. 2007; Yenicesu et al. 2010). Considering the importance of the problem thrombophilia in pregnant women and its association with recurrent pregnancy loss (RPL), analysis of polymorphisms of genes involved in thrombophilia can be useful.

Methods: We investigated the frequency and association between ten polymorphisms of seven thrombophilia genes and RPL in an Iranian population. This case-control study was conducted on 200 women with recurrent pregnancy loss and also on 200 women with at least one successful pregnancy as the control group. Using PCR-RFLP, DNA from samples were analyzed for carrying A5279G, A4070G, and FV Leiden of factor V; FXIII

(Val34Leu); FII (A20210G); BF (−455 G⁄A); ITGB3 (1565T⁄C); 677C/T and 1298A/C of MTHFR; and PAI-1 (−675 I/D, 5G/4G) polymorphisms.

Results: In this study, 200 healthy people as controls and 200 patients were examined and in some cases, the results showed different results compared with studies conducted in different populations with respect to relation between thrombophilia gene polymorphisms and the risk of RPL. The BF(−455 G⁄A), MTHFR (677 C⁄T, 1298A⁄C), PAI-1 (−675 I/D,4G⁄5G), FV Leiden, FV (A5279G), FXIII (Val34Leu) polymorphisms, which had shown positive relation, and ITGB3 1565T⁄C were the polymorphisms with negative relation to RPL. But in this study it is indicated that there is no significant association between FII (A20210G) and FV (A4070G) polymorphism and RPL. All the data acquired from the RPL patients in this experiment illustrate the importance of screening thrombophilia. Nevertheless, more studies on large-scale populations may be needed to identify novel genetic variants.

Conclusion: In this study, bias is unlikely to be present for the following reasons. First, because all the women were of the same ethnic origin and lived in the same geographic area, variations in the frequency of gene mutations were minimized. Second, interpretation bias was avoided by having the laboratory diagnosis made by technicians who were unaware of the characteristics of the study participants. However, in order to better understand the pathobiology of thrombophilia in RPL disease, further studies are needed on larger scale populations and identify novel genetic variants and the interaction of these variants with each other and the environment.

Keywords: Recurrent pregnancy loss; gene polymorphisms; thrombophilia

Association of Acquired Factor VIII Deficiency with COVID-19 (Research Paper)

Mohammad Shayestehpour,[1,*]

1. Department of Microbiology and Immunology, Faculty of Medicine, Kashan University of Medical Sciences, Kashan, I.R. Iran

Introduction: Acquired factor VIII (FVIII) deficiency, or acquired hemophilia A (AHA), is a rare autoimmune disease characterized by severe bleeding. 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). We present here a case of acquired factor VIII deficiency associated with COVID-19.

Methods: A 34-year-old woman with abnormal uterine bleeding was referred to the hospital ten days after cesarean delivery. Platelet count (PLT), prothrombin time (PT), partial thromboplastin time (PTT) tests were in the normal ranges, but the hemoglobin (Hb) level was reduced to 7 g/dL. Administration of Fresh-Frozen Plasma (FFP), packed cell (P.C), and recombinant factor VII could not control bleeding. She was discharged and returned to the hospital nine days later with symptoms of fever, bleeding, and respiratory failure. The patient underwent hysterectomy, discharged and returned to the hospital nine days later with symptoms of fever, bleeding, and respiratory failure.

Results: She was intubated, and had a heart rate of 110 per min and blood pressure of 100/70. The patient's body temperature was 38℃ and antibiotics (vancomycin and meropenem) were started. She had Hb level of 6.5 g/dL, PLT of 150000/mm3, and PTT of 75 s. Polychromasia was observed in the patient's peripheral blood smear (PBS) while blast cells and schistocytes were not seen. Hemoperitoneum detected on sonography, and abdominal angiography was normal. The patient underwent laparotomy and splenectomy. Administration of FFP and P.C increased PTT to the normal range, Hb to 9 g/dL and decreased the bleeding. SARS-CoV-2 was detected in the patient's sample by reverse-transcription polymerase chain reaction test (RT-PCR), although she had a normal chest CT. The sedimentation rate (ESR) and level of C-reactive protein (CRP) were normal and lymphopenia was not happened. The patient was discharged with good general condition and PPT of 45 s without receiving any treatment for COVID-19. She was readmitted to the hospital 4 days later, that result of laboratory tests as fallow: White Blood Cells (WBC) 23000/mm3, PLT 450000/mm3, lactate dehydrogenase (LDH) 700 U/L, Hb 5.8 g/dL, PT 14s, PTT 95s. In PTT mixing study, PTT decreased to 50s without incubation time and to 73s after 3h

incubation in 37℃. In PT mixing study, PT was 12.9s immediately after mixing test, and it increased to 17s, 3h after incubation. The sonography showed a hematoma with 500 cc of blood (diameter of 10 cm) in the hypogastric region. In addition, a hematoma with diameter of the 13 cm was observed near to the gastric. After administration of P.C (one unit), FFP, recombinant factor VII, IVIG (34g daily for 5 days), dexamethasone (24mg/day), vancomycin and meropenem the following laboratory data were obtained: Hb 8.2 g/dL, PTT 41s, INR 1.43 and WBC 22100/mm3. Anti-factor VIII antibodies were detected in serum (180 BU) and level of factor VIII was 1%. Treatment with cyclophosphamide (100mg bidaily) was initiated. The patients under treatment with dexamethasone and cyclophosphamide had a PTT ranged from 50 to 70 s without bleeding. In final sonography, the diameter of hematoma was decreased. The patient was discharged on 75 mg of prednisone daily and 100mg of cyclophosphamide bidaily. She had not fever and had Hb of 11 g/dL and PTT of 71s. Anti-factor VIII antibodies were undetectable and factor VIII activity was normal.

Conclusion: Infection with SARS-CoV-2 can be associated with an acquired factor VIII (FVIII) deficiency in human. Performing PTT mixing test in cases of COVID-19 with a prolonged PPT and unexplained bleeding is recommended.

Keywords: Coagulation, Factor VIII, COVID-19, Hemophilia A

Association of ART3 rs6836703 polymorphism with non-obstructive azoospermia in Iranian men. (Research Paper)

Pouria Yousefi,[1,*] Amir amiriyekta,[2] Mehdi Shamsara,[3] Elmira Vanaki,[4] Morteza Daliri Joupari,[5]

1. National Institute of Genetic Engineering & Biotechnology
2. Royan Institute
3. National Institute of Genetic Engineering & Biotechnology
4. National Institute of Genetic Engineering & Biotechnology
5. National Institute of Genetic Engineering & Biotechnology

Introduction: According to the definition of the World Health Organization, if a couple does not have children within one year after unprotected sexual activity, they suffer from infertility, which affects infertility in both men and women. Various factors affect male infertility, about 15 to 30% of which are genetic abnormalities. It is also predicted that most unknown cases of infertility are based on a genetic defect. Studies on the ART3 gene have shown that it is associated with NOA. Therefore, in this study, we investigated the association of ART3 rs6836703 polymorphism with NOA in the Iranian infertile male population.

Methods: In this study, 100 genomic DNA samples of NOA individuals and 100 samples of control (fertile) individuals were received from Royan Research Institute, and then using Tetra ARMS-PCR technique, rs68367033 polymorphisms were examined in both groups.

Results: The results showed that the frequency of mutant A allele in the patient group was higher than the control group, but in both groups, the frequency of the normal G allele was higher than the mutant allele and no significant relationship was observed between the patient and healthy groups (P -0.067 and OR-0.672). Also, the findings about genotype showed that AA genotype is 16% in patients and 7% in control group and normal GG genotype is 45% in patients and 53% in control group, which indicates the higher frequency of mutated genotype in patients and The frequency of normal genotypes is higher in healthy individuals.

Conclusion: The study of rs6836703 polymorphic relationship in Iranian male population did not show a significant relationship with NOA.

Keywords: Infertility, NOA, Non-obstructive azoospermia, ART3 gene, polymorphism rs rs6836703

Association of Gly84Glu (251G / A) mutation in HOXB13 gene with prostate cancer of Iranian men (Research Paper)

SeyedAli Abdollahi Oskouei,[1] Zahra TahmasebiFard,[2,*]

1. Department of Biology, Bonab Branch, Islamic Azad University, Bonab, Iran
2. Department of Biology, Roudehen Branch, Islamic Azad University, Roudehen, Iran

Introduction: HOXB13 is a homeodomain transcription factor that is linked to recurrence following radical prostatectomy. While HOXB13 Regulates Androgen receptors (AR) functions in a context-dependent manner, its critical effectors in prostate cancer (PC) metastasis remain largely unknown. This gene belongs to the homeobox gene family and encodes a transcription factor. Genes of this family are highly conserved among vertebrates and essential for vertebrate embryonic development. Men who inherit a rare genetic variant in HOXB13 (G84E or rs138213197) have a 10-20-fold increased risk of prostate cancer. The present study investigates the relationship between Gly84Glu (251G/A) polymorphism and prostate cancer in Iranian women.

Methods: This case-control study analyzed blood samples from 100 patients with prostate cancer as well as 100 healthy men. Genomic DNA was extracted using the salting-out method. After design the suitable primers for polymorphism, the samples were amplified for the considered segment, and genotypes of the participants were determined by PCR-RFLP.

Results: Both groups were at the age range of 58 to 70; the mean age of participants was 60.54±1.13 years in the cancer group and 58.17±1.13 in the control group. According to the genotype counting, Individuals with prostate cancer had the following genotypes : GG 61% , AA 27%, and AG/GA 12% compared to the control group that had genotypes GG 12%, AA 6%, and AG/GA 6%. There were meaningful differences in the frequencies of homozygotes GG (P=0.001) and AA (P=0.007) between patients and controls. By logistic regression analysis, individuals carrying the AA genotype were a 3.03 times more chance to develop prostate cancer (p=0.004, OR:3.025, CI95%: 1.420-6.446). According to the Hardy–Weinberg equilibrium, the frequency of allele G was 0.67 in the cancer group and 0.85 in the control group. The frequency of allele A was 0.33 in the cancer group and 0.15 in the control group. With logistic regression, the chance of developing prostate cancer in carrying Allele A was increased 2.791 times (p=3.7×10-5, OR:2.791 , CI95%: 1.714-4.544).

Conclusion: Polymorphism Gly84Glu (251G/A) in gene HOXB13 is related to the risk of developing prostate cancer and it is likely one of the major factors in its occurrence.

Keywords: Gly84Glu mutation, HOXB13, polymorphism, Prostate cancer

Association study Between rs7975232 Polymorphism in Vitamin D Receptor Gene and Periodontitis by Tetra Arms PCR (Research Paper)

Nafiseh Tavakoli,[1] Elham Siasi,[2,*] Kumars Amini,[3]

1. Master of Genetics, Department of Genetic, Faculty of Biology Sciences, North Tehran Branch, Islamic Azad University, Tehran, Iran
2. Master of Genetics, Department of Genetic, Faculty of Biology Sciences, North Tehran Branch, Islamic Azad University, Tehran, Iran
3. Associate Professor, Department of Microbiology, Faculty of Biology Sciences, Saveh Branch, Islamic Azad University, Saveh, Iran

Introduction: Periodontitis is an inflammatory multifactorial disease in tooth tissues. Many genetic reasons and environmental factors are caused this disease. Vitamin D deficiency, is determined related to periodontitis disease risk. In this study was investigated of the association between rs7975232 polymorphism in vitamin D Receptor gene and periodontitis in Iranian patient and control groups.

Methods: Blood samples from 100 samples (50 patients and 50 controls group) were selected and DNA from samples was extracted by DNA extraction kit. Genotyping was used by Tetra Arms PCR method. Tetra Arms PCR genotyping results was confirmed by sequencing. Then results were statistical analyzed by SPSS (Statistical Package for the Social Sciences) software.

Results: Frequency of AA, AC and CC Genotypes were 25 (50%), 14 (28%), and 11 (22%) in cases, and 26 (52%), 16 (32%) and 8 (16%) in controls, respectively. AA genotype was the highest genotype between patient and control groups. Statistical analysis showed no significant association between this polymorphism and periodontitis disease in the studied samples (p=0.67).

Conclusion: This finding showed there was not significant association between rs7975232 polymorphism in vitamin D Receptor gene and periodontitis disease in the Iranian studied samples. For confirming of this results, further studies with large sample size and different types of population, was recommended.

Keywords: Periodontitis disease, Single nucleotide polymorphism, Vitamin D receptor, Tetra arms-PCR.

AZFc deletions and males infertility (Review)

Fatemeh Mohebi,[1,*] Mina Soleimani,[2] Hanane Hamidi,[3]

1. Molecular Medicine Research Center, Hormozgan Health Institute, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
2. Iran University of Medical Sciences, Tehran, Iran
3. Khalkhal University of Medical Science, Khalkhal, Iran

Introduction: Introduction: Infertility globally affects approximately 10-15% of couples which male factor infertility is a contributor in 50% of cases. Genetic defects are one of the factors that can cause male infertility. It has been estimated that the frequency of Yq microdeletions in infertile men is approximately 330 times more than its occurrence among infertile men in the population. Most commonly Yq deletions recur in Azoospermia Factor (AZF) loci and it has been shown that the AZFc is the most frequently deleted locus in infertile men.

Methods: Methods: At Pub Med and Science Direct, we examined 20 studies conducted from 2015 to 2021 by using key- words male infertility, Y chromosome, AZF, and microdeletion.

Results: Results: The AZFc locus is made out of repeated sequences and palindromes consequently making it most susceptible to deletions. AZFc involves a complete deletion (b2/b4 region) and many partial deletions that include b1/b3, b2/b3, and three variations of the gr/gr. 3 studies have reported an association between b1/b3 deletion and male infertility. 12 studies reported a poor (but statistically significant) correlation of b2/b3 deletion and male infertility. There has been a lot of controversies over the association of gr/ gr deletion with male infertility. It was demonstrated that the gr/gr deletion may not be a direct cause of infertility, but it disrupts the spermatogenesis process, which leads to a decrease in sperm count. It has been shown that the frequency of gr/gr is twice in the infertile men.

Conclusion: Conclusion: These observations indicate that regardless of the type of deletion, the loss of gene copies in AZFc increases the sensitivity of an individual to a decrease in sperm count.

Keywords: Keywords: male infertility, Y chromosome, AZF, microdeletion

Bacterial bioreactors as biodegrading tools (Review)

Soha Mokhtari garakani,[1,*] shima Mokhtari garakani,[2]

1. payam - e-noor university
2. payam - e-noor university

Introduction: Textile industry is a water consumer which produce enormous volume of harmful dyes and chemicals into water. therefore, finding cost effective, efficient and ecofriendly approaches are essential.in this review we try to present studies on the bacterial bioreactors to biodegrade the groups of azo dyes family And some consortium do to the fact that in some cases only one strain of bacteria is not sufficient.

Methods: one of the most Practical dye in textile industry is azo family. Wide color range, Ease of utilize, strong attachment to the material fibers, qualified colors and proper energy consumption makes azo dyes one of textile industry s favorite dyes family with the chromophoric azo group. The resistance of Complex aromatic structure of azo dyes family gives them High toxicity level which threatens human health and the environment. Therefore, the proper, cost efficient and ecofriendly approach to eliminating these contaminants are necessary. Bacteria as Microorganisms which produce oxidoreductive enzymes are one of the Eco friendly bioreactors for dyes biodegradation.

Results: Using bacterial tools to biodegrade Azo family dyes has been taken into consideration by groups of researchers. D.C. Kalyani et al. studied Pseudomonas sp. SUK1. Strain as one of Pseudomonas species, and its effect on textile dyes. they announced that Pseudomonas sp. SUK1. Can biodegrade 52% of the Reactive Red 2 from sulfonated azo dye family in the vast range. contrary to previous studies On P. luteola, P. mirabilis, K. rosea and Pseudomonas sp. evaluate the product toxicity and announced the change of the Reactive Red 2 into a non-toxic product under Pseudomonas sp. SUK1 treatments. Samta Saroj et al. studied a group of azo dyes family (Acid Red 183 (AR 183), Direct Red 75 (DR 75) and Direct Blue 15 (DB 15)) at 95–100% biodegradation level by Penicillium oxalicum SAR-3. they announced that manganese peroxidase presence implied enzymatic activity in decolorizing process. Muhammad Ikram et al. announced that a list of bacteria such as orand Clostridium sp., Bacteroides sp., Sphingomonas xenophaga BN6, Butyrivibrio sp., Eubacterium sp., are decolorizing azo dyes in anaerobic conditions. they announced that decolorization of reactive red 22 dye by Pseudomonas luteola as well as P. luteola biofilm in 89% level. they also announced that S. arlettae strain decolorized four members of azo dyes family at 97% level. In another study Manjinder Singh Khehra et al, researched on a bacterial consortium that contains Pseudomonas sp. Stenotrophomonas sp. and Bacillus sp. as a biodegradation treatment of

synthetic dye (Acid Red 88) in the anoxic-aerobic conditions. they resulted in 98% decolorization and 95% chemical oxygen demand (COD) removal. In another study HeFang et al. introduced A microbial consortium obtained from a Pseudomonas 1-10 and white-rot fungus 8-4. They designed this consortium for Direct Fast Scarlet 4BS decolorization as a water-soluble dye from azo family. the result Show that the Pseudomonas 1-10 treatment, in three condition of incubating- (a)continuous static incubation, (b)continuous shaking incubation, (c)static incubation then change to shaking incubation- presents 90%, 65% and 84% biodegrading effects respectively. On the other hand, the consortium treatment presents almost 100% biodegrading effect.

Conclusion: textile industries pollution is a considerable Issue nowadays. The original and synthetic dye diffusion into water makes human health threats and environmental hazard. and the massive amount of this diffusion demands an urgent solution. Bacterial treatments are cost effective, ecofriendly and efficient approaches to dyes degradation. The different studies on bacterial decolorization treatment show us The success of some strains as biodegradation tools of textile dyes although different kinds of bacterial consortiums present more prominent results.

Keywords: biodegradation-bioreactors-consortium

Beneficial effect of daidzein on renal dysfunction, apoptosis and fibrosis in the ovariectomized rat: Role of angiotensin receptors and microRNAs (Research Paper)

Majid Askaripour,[1,*] Hamid Najafipour,[2] Shadan Saberi ,[3] Fariba Poosti,[4] Saleh Yazdani ,[5] Soodeh Rajabi,[6]

1. Department of Physiology, School of Medicine, Bam University of Medical Sciences, Bam, Iran.
2. Department of Physiology and Pharmacology, and Cardiovascular Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
3. Department of Physiology and Pharmacology, Afzalipour Medical Faculty and Physiology Research Centre, Kerman University of Medical Sciences, Kerman, Iran
4. Laboratory of Molecular Immunology, Department of Microbiology, Immunology and Transplantation, Rega Institute for Medical Research, KU Leuven, Leuven, Belgium
5. VIB-KU Leuven Center for Microbiology, Leuven, Belgium
6. Department of Physiology and Pharmacology, and Cardiovascular Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran

Introduction: Chronic kidney disease (CKD), accompanied by renal dysfunction, fibrosis, and apoptosis, is highly prevalent in postmenopausal women. Here, we tested the hypothesis that the isoflavone daidzein may ameliorate renal dysfunction, apoptosis and fibrosis through angiotensin II type 1 (AT1R) and angiotensin 1-7 (MasR) receptors in association with microRNAs 33a and 27a.

Methods: Two weeks before the initiation of the experiments, rats (n=84) underwent ovariectomy (OVX). Then, unilateral ureteral obstruction (UUO) was performed in OVX rats, and animals were allocated to the following groups (n=21): sham vehicle (dimethyl sulfoxide; DMSO), UUO vehicle, UUO+17β-estradiol (E2), and UUO+daidzein. Each group encompassed three subgroups (n=7) treated with saline, A779 (MasR antagonist) or losartan (AT1R antagonist) for 15 days. The fractional urine excretion of sodium (FENa+) and potassium (FEK+), renal failure index (RFI), renal interstitial fibrosis (RIF index), glomerulosclerosis, renal miR-33a and miR-27a expressions and their target genes were analyzed. Apoptosis was measured by performing cleaved caspase-3 immunohistochemistry.

Results: UUO increased kidney weight, FENa+, FEK+, urine calcium, RFI, RIF index, glomerulosclerosis, and cleaved caspase-3. Moreover, expression of renal miR-33a and miR-27a, collagen3A1 and fibronectin mRNA and

protein were upregulated post-UUO. Daidzein and E2 treatment with or without losartan or A779 alleviated renal dysfunction, apoptosis and fibrosis

Conclusion: Compared to E2, daidzein efficiently ameliorated renal dysfunction, apoptosis and interstitial fibrosis through modulation of miR-33a and miR-27a expression and their crosstalk with AT1R and MasR. Therefore, daidzein might be a promising candidate for treating CKD in postmenopausal and older women.

Keywords: Daidzein, ovariectomy, apoptosis, renal fibrosis, angiotensin receptor, microRNAs

Benefits and Applications of Moringa oleifera in Food and Pharmaceutical Industries (Review)

Zahra Beig-Mohammadi,[1,*] Forough Hashemi,[2]

1. Department of Food Science and Technology, North Tehran Branch, Islamic Azad University, Tehran, Iran.
2. Department of Food Science and Technology, North Tehran Branch, Islamic Azad University, Tehran, Iran.

Introduction: Moringa oleifera is a plant native to the Arabian and southern Himalayas, Northeastern India, Pakistan, and Afghanistan. But today, it has spread to many tropical and subtropical countries, growing in South America, India, Saudi Arabia, and the Pacific and Caribbean islands. It is known as the miracle tree. This plant Has parts of the root, stem, gum, leaf, fruit (pods), flowers, and Seeds, with Medicinal, nutritional, antibacterial, antioxidant, antidiabetic, anticancer, and health-promoting properties. M.oleifera in different countries as a source of Digestible proteins, calcium, iron, potassium, zinc, magnesium, copper and vitamins such as vitamin A, B, C, D, E, folicAcid, pyridoxine, Nicotinic acid, Bioactive molecules such as β-carotene, α-tocopherol and chemicals such as tannin, sterols, trinoids, flavonoids, saponins, anthraquinones, alkaloids, and sugar reducers along with anticancer agents such as glucosinolate, isothiocyanate, are compounds of Glycoside. The phytochemical composition of each part of the plant is summarized, pods (flavonoids, tannins, terpenoids, and saponins), leaves (flavonoids, phenoli acids, lignans, alkaloids, dietary fibre, proteins) , seed (polyphenols, fatty acids, dietary fibre, proteins), stems (polyphenols, moringa gum, proteins), flowers (flavonoids, glucosinolates, proteins) leaf powder, as an antioxidant enrichment, increases the overall nutritional quality Along with the sensory properties and durability of the product.

Methods: Some researchers have shown that food products can be fortified with M.oleifera to provide Vitamins, minerals, essential amino acids, oils , and to maintain antioxidant capacity to increase their nutritional value. M.oleifera leaf powder or seed has been Used as an additive in a range of cereal and meat products. Enrichment of wheat-based bread with M.oleifera seeds powder (from to % 20 w/w to standard wheat flour)increased the protein (from 8.5 to 13.5 g/100g dry weight), ash (from 0.6 to 1.8 g/100g dry weight), fat (from 7.3 to 15.8 g/100g dry weight) and the amount of fiber (from 0.1 to 10.6 g/100g dry weight)and vitamin A, mineral contents. In contrast, moisture and total carbohydrate content decreased. However, only bread produced using %5 of M.oleifera seed powder was Characterized by similar overall acceptability concerning the %100 wheat bread. In particular, the fortification of white wheat bread with M.oleifera leaf powder (from 0 to %10 w/w to standard wheat flour), increased protein (from 13.6 to 14.6 g/100g dry weight),

ash (from 1.9 to 2.5 g/100g dry weight), and fiber content (from 13.7to 19.0 g/100g dry weight) of the bread samples.

Results: The most common substitution Level of M.oleifera leaf powder to base flours is from 10 to %15 w/w. The use of M.oleifera in meat and meat products has been prevalent due to its antioxidant and Bioactive compounds since consumers perceive them as safe and Included in the Generally recognized as safe (GRAS)category by Mashau et al. evaluated the Influence of different percentages(i.e., 1.2,3 and %5 of M.oleifera leaf extract on The nutritional profile and shelf life of mutton patties during 15day refrigerated Storage .showing that the inclusion of M.oleifera leaf extract significantly increased The protein(21.75 %), ash (2.73 %), total phenolic(41.96 mg GAE/g)and total Flavonoids (20.93mg CE/g)contents of the patties. In contrast, moisture and fat Content decreased during storage. Although, to a lesser extent than animal studies, Human studies have also been performed as related to the antidiabetic potential of M.oleifera extracts. In this regard, the research carried out by Fombang and Saa Investigated the antihyperglycemic effect of M.oleifera tea in both rats and Normoglycemic human volunteers using the oral glucose tolerance test. Overall, Both the animals and human volunteers consuming Moringa tea before the glucose Load did not register an increase in blood sugar compared to the control group. Also, the reduction in blood glucose was more evident at the lowest tea strength (200 mL) Than when using the highest one (400 mL).

Conclusion: However, most of the nutritional properties of this plant are related to glucosinolates and Isothiocyanates. M.oleifera seeds are used to remove heavy metals such as arsenic in groundwater Due to their antimicrobial and coagulant properties in water treatment. Moringa has remarkable Potential due to its nutritional, antioxidant, antidiabetic, anticancer properties. Therefore, they can Be used as a natural substance in various food systems. But still technological and sensory aspects For more information about using Moringa-derived ingredients are required for fortified foods.

Keywords: Moringa oleifera, Antioxidants, Antidiabetic effect, Anticancer

Bimodal silver nanoparticles modified with targeted biocompatible chitosan polymer for intelligent colon cancer theranostic (Research Paper)

Fatemeh Mahboubi,[1] Javad Mohammadnejad,[2] Sepideh Khaleghi,[3,*]

1. Department of Biotechnology, Faculty of Advanced Science and Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.
2. Department of Life Science Engineering, Faculty of New Sciences & Technologies, University of Tehran, Tehran, Iran.
3. Department of Biotechnology, Faculty of Advanced Science and Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.

Introduction: Colorectal cancer is the third most common cancer worldwide, the second leading cause of cancer-related death, and the leading cause of death from gastrointestinal cancer. The lack of early detection methods is one of the main reasons for the high mortality rate caused by this disease. Conventional imaging techniques are incapable of distinguishing benign tissue from malignant tissue, resulting in misdiagnosis or late-stage diagnosis. Therefore, the development of novel technologies to diagnose colorectal cancer accurately and promptly minimizes mortality from the disease. Surface-enhanced Raman spectroscopy (SERS) is one of the most precise techniques for molecular imaging, with advantages, such as non-invasion, high sensitivity, and specificity. Silver nanoparticles improve Raman spectroscopy signals due to the intensification of surface plasmons. Nanoparticle stability can be enhanced by adopting the Metal-Organic Framework (MOF). Due to numerous structural topologies, highly specialized surfaces, and ordered crystalline pores, MOFs are the appropriate choice for fixing metal NPs. Our aim in this project is the synthesis of Chitosan decorated MOF-Silver nanocomposites conjugated with folic acid for targeted diagnosis of colon cancer by Surface-enhanced Raman spectroscopy (SERS).

Methods: Silver nanoparticles were synthesized by the green method using cyanobacterium spirulina extract. The synthesized silver nanoparticles were attached to the Metal-Organic-Framework (MOF) by different methods. The physical and chemical properties of nanocomposites were investigated using TEM, SEM, and XRD imaging methods that evaluate the morphology of nanocomposites. The hydrodynamic size of nanocomposites was determined by the DLS test. The surface charge of nanocomposites was evaluated by zeta potential test. Chitosan was conjugated with folic acid and the accuracy of covalent bonds and interactions in nanocomposites at each step was confirmed by the FTIR method. The crystal structure of nanocomposites was evaluated by the XRD method. Raman signals of nanocomposites were analyzed by Raman spectroscopy. The toxicity of MOF@Silver

nanocomposite at different concentrations of MTT treatment on HCT116 colon cancer and HGF human normal cell lines was also evaluated. Finally, the results will be evaluated with SPSS software and t-test and one-way ANOVA.

Results: According to the findings of a morphological investigation, chitosan nanoparticles targeted with folic acid have an appropriate size and a spherical appearance. The crystallized structure of nanocomposites was evaluated by XRD. The covalent attachment in MOF structure and the confirmation of silver nanoparticle synthesis were assayed by FT-IR. The Surface-enhanced Raman spectroscopy of MOF@Silver nanocomposites which is synthesized by different methods shows different signaling abilities according to the process of preparation. The MTT assay was used to demonstrate the lethality of this nanocomposite in HCT116 colon cancer and HGF human normal cell lines. The application of folic acid-targeted chitosan-coated MOF-Silver nanocomposite modifies Raman spectroscopy signals dramatically, and it is toxic to colon cancer cells (HTC116). However, the cytotoxicity of Folic acid targeted MOF-Silver-chitosan nanocomposites is reduced in face of human normal HGF cell line.

Conclusion: SERS (Surface Enhanced Raman Spectroscopy) is a beneficial and safe method for detecting biological targets like cancerous cells. We show that a folic acid-conjugated, Raman-labeled chitosan MOF@Silver nanocomposite can be used to identify folate receptor positive colon cancer cells in this study. Moreover, the nanocomposites have acceptable biocompatibility against normal cell line. Nanoparticle-based Surface Enhanced Raman Spectroscopy (SERS) analysis offers a lot of potential for accurate colon cancer diagnosis, and it could help save a lot of colon cancer patient's lives throughout the world.

Keywords: Colon cancer, Surface Enhanced Raman Spectroscopy, MOF, Silver Nanoparticle, Folic acid

Bioethanol and effect on world life (Review)

Parsa Karpasand,[1,*] Aria Karpasand ,[2]

1. mofid high school
2.

Introduction: Due to energy crisis, pollution and environmental impacts resulted from the utilization of fossil fuels people have turned to renewable energy. The utilization of biofuels helps to protect the environment. Bioethanol presents a potential path to prevent global political instability and environmental problems driven by the reliance on fossil fuels. Greenhouse gas emissions from fossil fuel combustion cause global warming, acid rain, climate change, ozone depletion, and biodiversity damage. The depletion of fossil fuel reserves and the increase in pollutants and the resulting climate change in the Earth's atmosphere have made the production and use of renewable energy sources that are less polluting an inevitable necessity in the present age. It is estimated that the world's population will reach more than 2 billion by the year 8, and to maintain political and social security, 5% more fuel, 4% more food, 2% more water and 2% less carbon dioxide emissions are needed. Therefore, it is important to use fuel systems without producing carbon dioxide and without endangering food and water resources. This research focuses on the production of ethanol using cellulosic, sucrosic and fungal sources with a purity of 70 to 90%. Some applications of bioethanol include pharmaceutics, fuel cells, chemical synthesis, making solutions and similar applications in medicine

Methods: Ethanol or ethyl alcohol is a clear and colorless liquid that easily burns and water and carbon dioxide are produced as a result of its combustion. Ethanol can be produced by both synthetic and fermentation methods, where ethylene is utilized in the synthetic method. The main purpose of the researchers of this paper is to produce various bioethanol's using fruit waste and yeast method in order to discover the superior class of ethanol in terms of time, cost, type of materials, abundance of raw materials in Iran and etc. Some effective factors on the improvement of ethanol quality include: type of yeast (very important), type of sugar, distillation type, type of airlock, storage site among others. When all the factors are checked, the product with highest percentage and lowest harms is identified as the best biofuel in the fermentation method

Results: In this diagram, the amount of methanol or fuel consumption can be observed and it shows that at the beginning of the process, a lot of energy is consumed and when time passes, the amount of methanol burning decreases and finally becomes constant. This diagram indicates the amount of product or output which increases during first 3 hours and after that, it decreases due

to the decrease in the amount of oxygen into the retort. To prevent the process from degradation, open one of the retort's necks to remove water vapor and increase the amount of oxygen into the tank, and after a few minutes close the retort's neck and continue the process (If the whole process is done with the open neck, the temperature rises significantly, so that a large amount of bioethanol is released with water vapor) In the intersection of two graphs, i.e. the equilibrium point, which is achieved about 1 hour after the start of the process, the output become equal to the input, and after the equilibrium point onwards, the yield reaches to 100 and whole-profit situation is obtained. This diagram can be used to measure the boiling point of the solution of water, sucrose and Saccharomyces Cerevisiae. The reason for the temperature decrease during seventh 30 minutes is the decrease in the amount of oxygen into the retort and the reason for the temperature increase during eighth 30 minutes is the increase in the amount of oxygen into the tank. According to this research, the lower the density, the higher is the consumption of fuel and high-density fuel causes the lower consumption of pollutant (petroleum product). Our proposed materials is diesel because it has higher density compared to other fuels and also, is abundant, accessible and inexpensive so that it decreases the cost of materials and the most important feature of diesel is that it has a higher flame temperature than other fuels.

Conclusion: According to the experiments, studies and investigation performed during this project, it was concluded that if 250 ml of sucrose and Saccharomyces Cerevisiae solution as well as 200 ml of input fuel were used for the bio-alcohol production process, a 100% yield is obtained, as can be seen in the above diagrams. Due to the special conditions of the coronavirus pondemy and the lack of testing facilities, we are intended to develop and improve the equipment and production processes, including the application of other materials such as fruit mixture, molasses, as well as other input fuels such as candle and thinner whose data will be added to this paper when the experiments are performed.

Keywords: bioalcohol-Bioethanol-Medical alcohol-Biofuel-microorganism

Bioinformatics Analysis of the miRNAs, Targeting RUNX3 Gene in Gastric Cancer (Research Paper)

Seyed Taleb Houseini,[1,*] Roya Bishe Kolai ,[2] Arash Sattari ,[3] Farkhondeh Nemati ,[4]

1. Department of Biology, Faculty of Basic Sciences, Qaemshahr Branch, Islamic Azad University, Qaemshahr, Iran
2. Department of Biology, Faculty of Basic Sciences, Qaemshahr Branch, Islamic Azad University, Qaemshahr, Iran
3. Department of Biology , Faculty of Basic Sciences , Islamic Azad University , Gorgan Branch , Golestan , Iran
4. Department of Biology, Faculty of Basic Sciences, Islamic Azad University, Qaemshahr Branch, Mazandaran,Iran

Introduction: Gastric cancer is the fourth common cancer in the world, and the second leading cause of death, due to cancer. It is known that gastric cancer can occur as a result of genetic and epigenetic alterations of the tumor-suppressing genes, regenerating genes, and adhesive molecules. As the miRNAs play a significant role in the regulation of the cellular procedures, this study aims to predict the miRNAs, targeting the RUNX3 gene, using bioinformatics tools.

Methods: After getting the RUNX3 protein chain from the NCBI database, the miRNAs targeting the gene were predicted using TargetScan, miRDB, and miRWalk databases using different algorithms.

Results: Based on the scoring system of the bioinformatics programs and considering the best targeting scores, hsa-miR-106b-5p , hsa-miR-130b-3p , has-miR-454-3p , has-miR-3666 , has-miR-4295 , has-miR-301b-3p were identified as miRNAs targeting RUNX3 gene . They were suggested for the practical studies in future.

Conclusion: Results from bioinformatics studies revealed that of the six miRNAs identified and are probably the targeting miRNAs specific for the RUNX3 gene , respectively . therefore it seems that these miRNAs can be a suitable candidate for in vitro studies in GC patients.

Keywords: Bioinformatics, Gastric Cancer, microRNA, RUNX3

Bioinformatics evaluation of the rs185294556 signaling pathway in VEGFA gene related to has-mir-24-3p- in individuals with COVID-19 (Research Paper)

Haniyeh Fooladinezhad,[1,*]

1. Department of genetics faculty of sciences shahrekord branch Islamic azad university, shahrekord iran

Introduction: CIVID-19 infectious disease is caused by the SARS-COV-2 virus, which is an acute respiratory virus. Although research on the disease is ongoing, findings have shown that altered gene expression as well as biomarkers such as miRNA and SNP can cause the disease. Studies and articles have shown that the VEGFA gene is highly expressed in people with COVID-19, which increases vascular permeability and fluid accumulation in the lungs, which is associated with inflammation. This gene is involved as one of the key and candidate genes in this disease.

Methods: For this reason, we used the NCBI, Mirbase, mirSNP, miRWALK2, DAVID, and KEGG sites to find bioinformatics information on miRNA and SNP genes and biomarkers.

Results: Has-miR-24-3p is predicted to target (G> T) rs4073460 in the 3 UTR region of the VEGFA gene in the COVID-19 inflammatory cycle inhibition pathway.

Conclusion: In the present project, according to bioinformatics predictions, has-miR-24-3p has a high binding power to VEGFA gene and if it binds, due to the negative regulatory function of this microRNA, the expression of the desired gene is expected to decrease and lead to decrease Vascular permeability, reduced fluid accumulation in the lungs and inflammation. This issue needs more laboratory studies.

Keywords: Keyword: COVID-19, miRNA, VEGFA, has-miR-24-3p, SNP

Biosensor to detect vaginal temperature and PH: A review study to promote women's individual health (Review)

Fereshteh Gholami,[1] Maryam Tadayyon,[2] Mohammad Reza Sanjabi,[3] Rahil Mosallanejad,[4] Seyyed Ebrahim Moosavifard,[5,*]

1. Student Research Committee, Bushehr University of Medical Sciences, Bushehr, Iran
2. Student Research Committee, Jahrom University of Medical Sciences, Jahrom, Iran
3. Student Research Committee, Jahrom University of Medical Sciences, Jahrom, Iran
4. Student Research Committee, Jahrom University of Medical Sciences, Jahrom, Iran
5. Department of Advanced Medical Sciences & Technologies, School of Medicine, Jahrom University of Medical Sciences, Jahrom, Iran

Introduction: One of the most important ways to assess a woman's personal health is to constantly monitor the pH and temperature of the vagina. Today, thanks to the development of biosensors and wireless sensors, the use of noninvasive methods with minimal intervention has become possible. These sensors can be used in various medical cases such as preventing premature birth, fertility diagnosis, ovulation and in diseases such as vaginitis. In this review, we provide an overview of recent applications of biosensors to detect vaginal pH and temperature.

Methods: In the forthcoming systematic review, the required data were collected using keywords and citing valid databases such as Scopus, PubMed, Google Scholar and ProQuest. The statistical population includes all studies conducted until 2021 in the field of measuring temperature and pH using biosensors. After reviewing the relevant findings and evaluating the quality of the data, 17 articles were analyzed.

Results: In this systematic review, three types of biosensors used to measure pH and temperature, including waterproof electronic decal (WPED), wireless sensor network (WSN) and OvulaRing were studied. Temperature biosensors are in vivo sensors for measuring intravaginal temperature over a long period of time. They are also equipped with disposable sensors compatible with the vaginal environment to monitor PH. The OvulaRing has the same function as a tampon. It is a vaginal ring that includes an integrated biosensor to continuously measure the temperature inside the vagina. WPEDs and WSNs, on the other hand, are non-allergenic and easy to connect to control vaginal sweating and PH. The characteristics of WPEDs include the following: adhesion, transparency, breathability, lack of moisture, flexibility and maintaining high accuracy against thermal and mechanical stresses.

Conclusion: According to research, among the advantages of these devices, low power consumption and low data for WPEDs, and flexibility and ease of use for OvulaRings, can be mentioned. We hope that by reducing the size of OvulaRings, it can be easier placed in the cervix, and with the development of WPEDs, the ability to measure health products will increase their use. Therefore, the progress of studies in this field is still needed, which helps women to improve personal health.

Keywords: Temperature, Biosensor, Vagina, Wireless technology.

Bloodstream infections in adult patients with malignancy, epidemiology, microbiology, and risk factors associated with mortality and multi-drug resistance (Research Paper)

Ali Amanati,[1] Zahra Shahhosein,[2,*]

1. Professor Alborzi Clinical Microbiology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
2. Division of Laboratory Hematology and Blood Banking, Department of Medical Laboratory Science, School of Paramedical Science, Shiraz University of medical Science, Shiraz, Iran.

Introduction: The main goal of this study is to find out about the epidemiology, microbiology, and risk factors related to mortality and multi-drug resistance Bacterial Bloodstream Infections (BSIs) in adult patients with cancer in Shiraz, Iran. A four-year trend of antimicrobial resistance pattern of BSIs is reported too.

Methods: A retrospective study was done on all adult patients with confirmed BSI who were referred to the center of oncology from July 2015 to August 2019

Results: During this four-year study, 2393 blood cultures were tested which 414 of them were positive and included in our study. Our patients were about 47.57 ± 17.46 years old, on average. The most detected bacteria were Gram-negative (GN) which were 63.3%(262), just 36.7%(152) of our positive cases were diagnosed with gram-positive bacteria. the most common gram-negative organism was Escherichia coli (123/262, 47%), followed by Pseudomonas spp. (82/262, 31%) and Klebsiella pneumoniae (38/262, 14.5%). The most frequently isolated pathogen among gram-positive bacteria (83/152, 54.6%) was Coagulase-negative staphylococci (CoNS). The most common Extended[1]Spectrum Beta-Lactamase (ESBL) producers detected in our study were Acinetobacter spp., Pseudomonas spp., E. coli, and K. pneumoniae (100, 96.2, 66.7%, and 60.7, respectively).). The most common carbapenem-resistant (CR) organisms isolated in this study were Acinetobacter spp., Pseudomonas spp., Enterobacter spp., E. coli, and K. pneumoniae (77.8, 70.7, 33.3, 24.4, and 13.2%, respectively). 39.3% of Enterobacterales and non-fermenter gram-negative BSIs were carbapenem-resistant. During these four years, from 2015 to 2018, the prevalence of multi-drug resistance (MDR) gram-negative BSI raised annually, not any changes was seen in the rate of mortality of gram-negative BSI which is about 20% (p-value = 0.55); although, patients with resistant gram-positive BSI had significantly higher mortality rate (35.4%, p-value = 0.001).

Conclusion: One of the most emergent problems, especially in oncology centers, is the prevalence of MDR gram-negative BSI. CR and ESBL-producing Enterobacterales and Pseudomonas spp are the most isolated pathogens. Just a few choices are available to treat MDRGN BSI effectively, especially in high-risk cancer patients, so the need for newer treatment is of great concern.

Keywords: Bloodstream infection, Multidrug-resistant gram-negative infection, Mortality

Breast Cancer following Diabetes Mellitus: truth or not? (Review)

AmirAli Moodi Ghalibaf,[1,*] Mina AkbariRad,[2] Nazanin Forghani,[3]

1. Student Research Committee, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
2. Assistant professor of Internal Medicine, Department of Internal Medicine, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
3. Student Research Committee, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

Introduction: Today, breast cancer (BC) becomes one of the most prevalent malignancies among women all over the world which causes millions of deaths every year. Unfortunately, too many exogenous and endogenous factors can increase the risk of BC incidence. In this term, some studies and evidence have been indicated that the human immune system status and hormonal changes of the body are strong potential factors in BC development. On the other hand, diabetes mellitus (DM) is known as the most common metabolic disorder worldwide that can be caused by autoimmune and hormonal dysfunctions in one's body. These joint processes in both BC and DM can potentially interact with each other and lead to one another disorder. Therefore, we are looking for the answer to the question of whether DM can lead to BC, or not?

Methods: A comprehensive search was done through electronic databases including PubMed, Scopus, Embase, and Web of Science with the keywords “Breast Cancer”, “Diabetes Mellitus” and other related MeSH terms up to July 2021. Original studies, review studies, and the references of the review studies were included. Finally, the related studies which investigated the possible relationship between BC and DM were reviewed.

Results: According to the reviewed of population-based epidemiological studies, it can be stated that diabetic Asian-American women have a significantly higher risk of BC; however, a wide range of the BC incidence between 15%-20% was reported in DM patients. On the other hand, some molecular mechanisms were potentially considered for the association between BC and DM, including activation of the insulin-like growth factors (IGFs) pathway, activation of the insulin pathway, chronic hyperglycemia leading to the Warburg effect, inflammatory cytokines, and the regulation of endogenous sex hormones. In detail, a decrease in estrogen plasma levels following insulin resistance can increase the risk of BC development. Moreover, studies determined that diabetic BC patients have more morbidities and mortalities, severe outcomes, need altered regimens for breast cancer treatment, and experience increased toxicity from cancer chemotherapy.

Finally, the studies on the BC staging indicated that DM has highly associated with stages III, IV, II, and I of BC, respectively.

Conclusion: Based on the mentioned finding, Breast Cancer can be significantly affected by Diabetes Mellitus in terms of incidence, outcomes, and management; however, more studies are needed to find out the exact molecular processes and other aspects of this association.

Keywords: Breast Cancer, Diabetes Mellitus, Insulin Resistance

Cancer Stem Cells: The past, present and future of cancer treatment (Review)

Nima Abedini,[1] Mahtab Moghaddam,[2] Zahra Kakavand ,[3] Mahmood Talkhabi,[4,*]

1. Department of Animal Sciences and Marine Biology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
2. Department of Animal Sciences and Marine Biology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
3. Department of Animal Sciences and Marine Biology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
4. Department of Animal Sciences and Marine Biology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran

Introduction: cancer is the result of accumulation of genetic and epigenetic changes that bring about uncontrolled cell division and invasive functions. This disease is one of the major medical challenges of the present century and has a considerable financial toll on health care systems. According to WHO statistics in 2020 alone, close to ten million individuals have died of cancer. In The past few decades, the focus of scientist, biologists and physicians has shifted to the concept of cancer stem cells (CSC) in order to explain the origins, metastasis and recurrence of cancers. Breast cancer is one of the most prevalent and important cancers in humans, affecting millions of women each year.

Methods: This study is a review, conducted by searching databases such as: Google scholar, PubMed, ResearchGate and Medline. 12 articles were chosen based on the keyword entries. Chosen articles fall into two categories: information and background on the subject and data on clinical trials.

Results: Cancer stem cells or CSCs were first identified in acute myeloid leukemia (AML). These cells are a small subset of neoplastic cells which can create tumors and sustain tumorigenic cell populations. The presence of these cells has been reported in melanomas, sarcomas, mammary tumors, colon cancers and other solid tumors. Another type of these cells called circulating cancer stem cells gain mesenchymal properties through a process called EMT which adds to their invasive and metastatic abilities. Depending on the tumor type these cells use different energetic and metabolic pathways, some use aerobic glycolysis and others use oxidative phosphorylation, fatty acid oxidation is the most common source of energy production in these cells. Due to the importance of these cells their identification and isolation is very important, some of the methods used in this process including the use of special dyes, establishment cultures and cellular markers. Multiple studies have suggested non-malignant stem or progenitor cells as the possible source

of these cells. Signal transduction pathways such as Wnt ،Notch ،Hedgehog and Hippo are crucial in creating and maintaining the special characteristics of these cells. Surface markers include CD44 ،CD133 ،CD34 ،CD38 and CD24 and Aldehyde dehydrogenase1 (ALDH1) is an intracellular marker. The presence of these markers is important for features such as carcinogenesis, invasiveness, stemness, self-renewal and migration. In cancer research breast cancer stem cell (BCSC) are cells that can form transplantable tumors and re- stablish heterogenic tumors. CD44+, ALDH1+ and CD24-/low are the most common markers of BCSCs. BCSCs are located in the tumor microenvironment which is rich in stromal cells, ECM, cytokines and growth factors.

Conclusion: Studying the right target for treatment and intervention is crucial in diagnosis, treatment and relapse prevention in cancers due to the high financial and human cost. In this study we review the latest findings in cancer stem cells and their different roles in cancer particularly in breast cancer.

Keywords: Cancer stem cells, Metastasis, Tumor, Signal transduction pathways, Cancer

Cannabinoid receptor type-1 and its correlation with CB1 gene polymorphism-1359G/A in ectopic pregnancy compared to the control group (Research Paper)

Bita Moudi,[1,*] Zahra Heidari ,[2] Azam Asemi-Rad,[3] Hamidreza Mahmoudzadeh-Sagheb,[4] Nadia Sheibak,[5] Marzie Ghasemi,[6]

1. 1Infectious Diseases and Tropical Medicine Research Center, Resistant Tuberculosis Institute, Zahedan University of Medical Sciences, Zahedan, Iran
2. 1Infectious Diseases and Tropical Medicine Research Center, Resistant Tuberculosis Institute, Zahedan University of Medical Sciences, Zahedan, Iran
3. Department of Anatomical Sciences, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran
4. 1Infectious Diseases and Tropical Medicine Research Center, Resistant Tuberculosis Institute, Zahedan University of Medical Sciences, Zahedan, Iran
5. Department of Histology, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran
6. Moloud Infertility Center, Ali ibn Abitaleb Hospital, Zahedan University of Medical Sciences, Zahedan, Iran

Introduction: Ectopic Pregnancy (EP) is one of the most important causes of maternal mortality. This study aimed to evaluate the immunohistochemical expression of the cannabinoid receptor type 1 (CB1) and its association with CB1 -1359G/A gene polymorphism (rs1049353) in the fallopian tubes in ectopic pregnancy compared to controls.

Methods: In this case-control study, 100 women with ectopic pregnancy (cases) and 100 women that underwent abdominal surgery due to the hysterectomy or uterine tubal ligation (healthy controls) were included. Genotyping of CB1-1359G/A polymorphism, tissue expression of CB1 at the protein and mRNA levels were studied using restriction fragment length polymorphism, immunohistochemical (IHC) method, and quantitative real-time polymerase chain reaction (qRT-PCR) analysis.

Results: Genotyping showed that in EP, the frequency of AA, AA+AG genotypes, and A allele was significantly higher than healthy control subjects (P=0.001). Also, patients with EP had significantly increased IHC expression of CB-1 compared to the control samples (P = 0.016). Patients with AA and AG genotypes had a significantly higher IHC expression of CB-1 compared to the GG genotype. Quantitative real-time PCR analysis showed that patients with EP had significantly increased expression of CB-1 compared to the control samples (P<0.001). Patients with AA and AG genotypes had higher significant mRNA expression of CB-1 compared to the GG genotype.

Conclusion: CB1 is likely to be effective in creating innate immunity in humans and can affect the process of EP in the fallopian tube. CB1 is also a pathological valuable factor in identifying the pathway of inflammation during ectopic implantation.

Keywords: cannabinoid receptor type-1, ectopic pregnancy, polymorphism, immunohistochemistry.

CAR-T Cell Challenges and Existing Solutions; Special Look at Solid Tumors (Review)

Ahmad Noei,[1] Shafieeh Mansoori,[2] Zahra Sharifzadeh,[3,*]

1. Immunology Department, Pasteur Institute of Iran, Tehran, Iran
2. Immunology Department, Pasteur Institute of Iran, Tehran, Iran
3. Immunology Department, Pasteur Institute of Iran, Tehran, Iran

Introduction: T cell engineering with the ability to express chimeric antigen receptor (CAR) is a dramatic breakthrough in the treatment of some malignancies, especially B-cell-related malignancies. Despite the brilliant results, there are limitations to the widespread use of this approach in relation to different clinical conditions and in general. Systemic complications associated with inflammatory cytokines that lead to pervasive inflammation, as well as on-target, off-tumor toxicity, are among many barriers to the performance of the CAR system. These problems include low persistence and tumor antigen escape of CAR-T cells. In addition, the optimal function of CARs in solid tumors is still an active area of research. Here we intend to briefly review the solutions from the perspective of synthetic biology, while pointing out the existing barriers.

Methods: In the present review, the data were extracted from google scholar papers between 2010 to 2021.

Results: The best results of CAR-T cell therapy have been associated with blood malignancies, specifically CD19 + ALL. However, antigen escape and cell survival of tumors in vivo reduce the effectiveness of treatment. Many engineering strategies have been developed to solve these problems. CAR design with the ability to identify multiple tumor associated antigens (TAAs) in the form of Tandem CAR or dual CAR is one of the solutions known to overcome the escape of antigen or heterogeneity of the tumors. These approaches, not only have the benefits of detection efficiency, but also can reduce off-target complications. In the split CAR approach, one receptor is designed against one TAA with CD3 signaling domain and another receptor against another TAA is designed with co-stimulatory domain (CD28 or 4-1BB). With a change in the second receptor against one TAA, an iCAR approach has been developed that detects activity-inhibitory signals if a non-tumor antigen is detected. The use of logic gating and / or conditional expression systems is another approach in which CAR-T activity depends on the expression of a target antigen and a specific transcription factor. In the Tandem CAR approach, two targeting domain (scFv) are placed in a single structure. In another design, cells that have the ability to secrete bispecific antibodies can be engineered, which are engineered molecules that have the ability to target two antigens simultaneously. Universal CARs are another

category that uses the modular structure to divide the classic CAR function into two separate parts. One part is to identify a switchable molecule or tag and the second part is the switching molecule itself. These modular CARs provide the ability to detect different antigens without the need for cell re-engineering. To increase the T cell persistence in vivo, less differentiated T cell subsets can be used that have a higher proliferation potential. Bystander cells, such as dendritic cells, can be engineered to secrete factors such as IL-12 and alter tumor microenvironment (TME) to help them survive longer in the body. The most important challenge in solid tumors is their trafficking. There are many physical and biochemical barriers to CAR-T-cells. Direct injection into the tumor site is known as a general solution. According to Synthetic biology, T-cells can be designed to secrete different chemokines. Stroma retargeting of T-cells including the designed CARs against FAP, or heparinase expressing CAR-T cells are another solution to enhance the CAR-T-cell infiltration. Suppressor TME is another major challenge in this area. The change in TME has been achieved by the Armored CAR approach, known as fourth-generation CARs. These cells are able to secrete or superficially express factors that alter TME in favor of optimal CAR function. This approach can also promote the microenvironment of the tumor in favor of the anti-inflammatory status and prevent systemic toxicity.

Conclusion: Exciting approaches are being developed to increase the effectiveness and scope of CAR-T Cell therapy. These approaches aim to promote the safety and efficacy of CAR-T-Cells. The effective solutions that synthetic biology has presented to us have raised hopes for the widespread use of these agents in the treatment of cancer.

Keywords: chimeric antigen receptor, solid tumor, cancer immunotherapy, synthetic biology, challenges

Causes of Rejection or Acceptance of Herd Immunity Against Covid-19 Infection (Review)

Omid salmani ,[1,*]

1. B.S of General Biology, Payamenoor University, Marand Branch, Iran

Introduction: Introduction: Herd immunity, often known as 'population immunity' is the indirect protection against an infectious illness that occurs when a population has gained immunological immunity as a result of a prior illness. The goal of this study is to look at the causes and outcomes of some research on herd immunity rejection and acceptance in Covid-19.

Methods: Search Method: The study method is based on the articles and reports of the World Health Organization on herd immunity against coronavirus, which were analyzed by searching scientific databases such as Science Direct, Springer, Google Scholar, PubMed.

Results: Results: the results of Many immunity tests which have been conducted in the Covid-19 indicate that herd immunity against Covid-19 is rejected for a variety of reasons. The most important one is that vast numbers of individuals must be exposed to the disease to determine their safety. On the other hand, it is unclear when safety will be achieved, and it is related to the number of people who become immune after COVID-19. In addition, many people will have to die to acquire herd immunity. It's unclear whether the infection provides immunity against future infections, or how long that protection will remain. According to the findings of some researches, there have also been cases of infections, were infected with COVID-19 for the second time. Furthermore, Coronavirus immunity is usually just temporary. For example, researches of survivors of the SARS-CoV (Severe acute respiratory syndrome coronavirus) epidemic indicated that patients who were IgG positive were kept immunity in >90% of the patients for 2 years. SARS-CoV antibodies were not found 6 years after infection, according to another study. Antibody responses in patients with asymptomatic or moderate illness are less than individuals with severe disease in numerous coronaviruses. There is currently no proof that those who have recovered from COVID-19 and have antibodies are immune to infection in the future.

Conclusion: Conclusion: The summary of the results of the researches, as well as the World Health Organization (WHO), believes 'herd immunity' through vaccination, not by allowing disease to spread through any segment of the population, as this would result in unnecessary cases and deaths. COVID-19 herd immunity should be obtained through vaccination rather than by exposing them to the organism that causes the disease.

Keywords: Key Words: herd immunity, Covid-19, infection

CD14+ monocytes and cardiovascular risk in patients with Hashimoto's thyroiditis. (Research Paper)

Monire Sadat Fazaeli,[1,*]

1. Department of Laboratory sciences, Iranshahr University of Medical Sciences, Iranshahr, Iran

Introduction: Hashimoto's thyroiditis is an autoimmune disease that is associated with high cholesterol levels and increased cardiovascular disease (CVD) risk. Atherosclerosis is prominently controlled by macrophages and CD14+ cells are proinflammatory monocytes that are expressed mainly by macrophages. In this study, we examine the relationship between CD14+ expression on monocytes and vascular risk.

Methods: Data and serum levels of TSH, FT4, Anti-TPO antibody, total cholesterol, LDL, HDL and expression level of CD14 on monocytes from 20 new untreated patients with Hashimoto's thyroiditis and 20 age- sex- and BMI-matched euthyroid controls were analyzed in a cross-sectional study. Quantification of CD14 expression on monocytes was done by flow cytometry. Lipoprotein ratios (total cholesterol/HDL cholesterol and LDL/HDL cholesterol ratios) were calculated to predict vascular risk. Then the relationships between these parameters were examined.

Results: Lipoprotein ratios and CD14 expression on monocytes was significantly higher in patients than in the control group (p = 0•001). There was a significant and positive relationship between Lipoprotein ratios and CD14 expression.

Conclusion: We found that CD14+ monocytes were significantly associated with cardiovascular risk in patients with Hashimoto's thyroiditis.

Keywords: Hashimoto's thyroiditis, Cluster of differentiation 14, Cardiovascular disease.

Cell Transplantation for the Treatment of Catecholaminergic Polymorphic Ventricular Tachycardia (Cpvt) (Review)

Elham Zendedel,[1,*] Shiva Asadpour,[2]

1. Department of Tissue Engineering and Applied Cell Sciences, School of Advanced Technologies, Shahrekord University of Medical Sciences, Shahrekord, Iran
2. Department of Tissue Engineering and Applied Cell Sciences, School of Advanced Technologies, Shahrekord University of Medical Sciences, Shahrekord, Iran

Introduction: Background: A method in which cells are used to repair or replace damaged tissues or cells is known as cell transplantation. Different types of cells may be used in the treatment of a number of diseases and disorders, according to emerging technologies. Catecholaminergic polymorphic ventricular tachycardia (CPVT) is an inherited genetic disorder a condition in which the heart beats irregularly (arrhythmia). Literature review: Scientists can investigate Ca2+ signaling parameters from human induced pluripotent stem cells (hiPSC-CMs) from healthy polymorphic ventricular tachycardia and aminergic catechol (CPVT1) that individuals have a new mutation p.F2483I on ryanodine receptors by differentiating cardiomyocytes from induced pluripotent stem cells (iPS-CM) (RyR2). Conclusion: Despite the fact that iPSC-CMs offer a lot of promise as a treatment for CPVT, immunological rejection caused by HLA mismatching is a problem, hence additional research is needed.

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Keywords: Induced Pluripotent Stem Cells (iPS-CM), Novel treatment, Inherited genetic disorder

Changes in motor performance and AMPA gene expression in the cerebellum of male rats during copper toxicity and treatment with vit C (Research Paper)

Zahra Nobakht Mobaraki,[1,*] Homeira Hatami Nemati,[2] Nazli Khajehnasiri,[3]

1. Department of Animal Biology, Faculty of Natural Sciences, University of Tabriz, Tabriz, Iran.
2. Department of Animal Biology, Faculty of Natural Sciences, University of Tabriz, Tabriz, Iran.
3. Department of Biological Sciences, Faculty of Basic Sciences, Higher Education Institute of Rab-Rashid, Tabriz, Iran.

Introduction: Copper is an essential transition metal that participates in the regulation of brain physiology, being a key structural component of various proteins and a co-factor for enzymes that are critical for brain function, including enzymes involved in antioxidant defense and cellular respiration. More recently, some reports have described the effect of copper at the synaptic level, where it modulates complex parameters such as Long Term Potentiation (LTP) and receptor pharmacology. Synaptic receptors may be targets for copper. α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptors (AMPARs) is a major type of ionotropic glutamate receptors involved in synaptic transmission. However, excessive activity of these receptors can be cytotoxic and thus their function must be precisely controlled. Indeed, it has been observed that copper inhibits AMPAergic neurotransmission. Thus, suggesting that copper has an acute modulatory role on the AMPA receptor in neurotransmission. There is evidence about up regulation of AMPA receptor expression and cell damage. We analyze the motor activity and changes in AMPA gene expression during neurotoxicity process of copper sulfate and evaluate the results of treatments using vitamin C in the cerebellum of male rats. Copper is critical for the Central Nervous System (CNS) development and function. In particular, different studies have shown the effect of copper at brain synapses, where it inhibits Long Term Potentiation (LTP) and receptor pharmacology. Paradoxically, according to recent studies copper is required for a normal LTP response. Copper is released at the synaptic cleft, where it blocks glutamate receptors, which explain its blocking effects on excitatory neurotransmission.

Methods: In this experimental study, 24 male Wister rats (250-300 gr) were randomly divided into 4 groups of 6 (n=6 in each). Control (normal saline), copper sulfate (10 mg/kg; i.p), vitamin C (160 mg/ kg; i.p), copper sulfate + vitamin C (160 mg/kg; i.p) for 10 days. On days 1, 5 and 10, coordination of rats' movements was assessed using the rotarod test 20 minutes after injection. After receiving treatments, the animals were decapitated and their cerebellum were removed and the expression of AMPA gene assayed using

RT-PCR Technique. One-way ANOVA and post-hoc Tukey test were used for data analyzing.

Results: Data analysis showed that the mean duration of resistance and remaining on the rotarod wheel in copper sulfate group was not significantly different from the control group ($p > 0.05$). While the mean duration significantly increased for the group of vitamin C compared to the control group ($p < 0.001$). The mean duration significantly increased for the group of copper sulfate + vitamin C compared to the control group ($p<0.05$). The mean duration significantly decrease for the group of copper sulfate compared to the vitamin C group ($p<0/001$). The mean duration significantly decrease for the group of copper sulfate compared to the copper sulfate + vitamin C group ($p<0.05$). The mean duration significantly increased for the group of vitamin C compared to the copper sulfate + vitamin C group ($p<0.05$). The expression level of AMPA gene in vitamin C and copper sulfate+ vitamin C group was not significantly different from the control group ($p > 0.05$). The AMPA gene expression increased in the copper sulfate group compared to the control group ($p<0.001$).The expression level of AMPA gene in copper sulfate was not significantly different from vitamin C group ($p > 0.05$). The AMPA gene expression increased in the copper sulfate group compared to the copper sulfate + vitamin ($p<0.01$).The expression level of AMPA gene in vitamin C and copper sulfate + vitamin C group was not significantly different from the control group ($p > 0.05$).

Conclusion: Our results indicate that copper increase the levels of AMPA gene expression and overload disturbed neuromuscular coordination. Also we think that the AMPA receptor may play a role in cerebellar injury caused by copper overload.

Keywords: Copper toxicity, vit C, NMDA gene expression, locomotor activity, rotarod test.

Changes in motor performance and NMDA gene expression in the cerebellum of male rats during copper toxicity and treatment with vitamin C (Research Paper)

Zahra Nobakht Mobaraki,[1,*] Homeira Hatami Nemati,[2] Nazli Khajehnasiri,[3]

1. Department of Animal Biology, Faculty of Natural Sciences, University of Tabriz, Tabriz, Iran.
2. Department of Animal Biology, Faculty of Natural Sciences, University of Tabriz, Tabriz, Iran.
3. Department of Biological Sciences, Faculty of Basic Sciences, Higher Education Institute of Rab-Rashid, Tabriz, Iran.

Introduction: Copper is an essential transition metal serving as an important cofactor for various enzymatic reactions and physiological activities. However, excess amounts of copper cause neurological abnormalities. There is evidence about up regulation of NMDA receptor expression and cell damage. We analyze the motor activity and changes in NMDA gene expression during neurotoxicity process of copper sulfate and evaluate the results of treatments using vitamin C in the cerebellum of male rats.

Methods: In this experimental study, 18 male Wister rats (250-300 gr) were randomly divided into 3 groups of 6 (n=6 in each). Control (normal saline), copper sulfate (10 mg/kg; i.p), copper sulfate + vitamin C (80mg/kg; i.p) for 10 days. On days 1, 5 and 10, coordination of rats' movements was assessed using the rotarod test 20 minutes after injection. After receiving treatments, the animals were decapitated and their cerebellum were removed and the expression of NMDA gene assayed using RT-PCR Technique. One-way ANOVA and post-hoc Tukey test were used for data analyzing.

Results: Data analysis showed that the mean duration of resistance and remaining on the rotarod wheel in copper sulfate group was not significantly different from the control group ($p > 0.05$). While the mean duration significantly decreased for the group of copper sulfate and vitamin C compared to the control group ($p < 0.001$). The expression level of NMDA gene in copper sulfate and vitamin C group was not significantly different from the control group ($p > 0.05$). The expression level of NMDA gene in copper sulfate group had a great rise compared to the control group ($p < 0.001$).

Conclusion: Copper overload disturbed neuromuscular coordination. Also we think that the NMDA receptor may play a role in cerebellar injury caused by copper overload.

Keywords: Copper toxicity, vit C, NMDA gene expression, locomotor activity, rotarod test.

Changing of Protein Concentration and Colloid Osmotic Pressure in Glomerular Capillaries Following a Decrease in Albumin-Globulin Ratio During Renal Filtration (Research Paper)

mohammad hossein Madahali,[1,*]

1.

Introduction: Renal Filtration, based on Starling Equation, is dependent on Hydrostatic Pressure (HP) and Colloid Osmotic Pressure (COP) between two sides of glomerular membrane in renal corpuscles. COP is related to plasma Total Protein Concentration (TP) and Albumin-Globulin Ratio (A/G). In this study, for different A/G, the mathematical relationship between COP and TP was developed in-vitro. Differential equation for changing COP and TP in glomerular capillaries was analyzed with numerical methods.

Methods: The results indicate that A/G affects the variations of TP and Net Filtration Pressure (NFP) in glomerular capillaries. The effect of A/G is also related to Mean Arterial Pressure (P), Inlet Plasma Flow (J), and Filtration Coefficient (K)

Results: For any value of S=K P/J, the variation of TP and NFP is inversely related to A/G.

Conclusion: Not only is NFP related to A/G, but also with a decrease in S, the filtration takes place along the glomerular capillary. With increasing S, the filtration is limited in the middle of capillaries, because pressures on each sides of glomerular membrane are approaching equilibrium

Keywords: renal kidney Glomerular

Chemical evaluation of Active Ingredients, Anti-oxidant and Anti-microbial Effects of Trachyspermum Copticum (Research Paper)

Ruholla rahimi nasab,[1,*] mostafa rahimi nasab,[2] Mohammad Javad Forouzani-Moghaddam,[3]

1. Bachelor of Biotechnology, Yazd University, Yazd, Iran
2. Bachelor of Biotechnology, Yazd University, Yazd, Iran
3. Msc of Food Microbiology, School of Paramedical, Iran University of Medical Sciences, Tehran, Iran

Introduction: Trachyspermum copticum as a medicinal plant has many therapeutic properties including; anti-flatulence, anti-emesis, anti- rheumatism and expectorant. The aim of this study was to identify active compounds, anti-oxidant and anti-microbial effects of Trachyspermum Copticum.

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 0.809µg/ml-1 and162.62mg/g-1 resepectively and the standard AATCC microbial test showed inhibitory effect of bacteria, especially K.pneumoniae and S.pyogenes indicated acceptable properties.

Conclusion: The result of this research indicated that the active ingrediebts of native Trachyspermum copticum harvested in Yazd province were much higher than the ones found in Trachyspermum copticum harvested in other places.

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

Chemical modification of polymer biomaterials for biomedical applications (Review)

Mina Morovati,[1,*] Mahsima Heydari,[2] Mahsa Heydari,[3]

1. Malek Ashtar university
2. Bioprocess Engineering Department, Institute of Industrial and Environmental Biotechnology, National Institute of Genetic Engineering and Biotechnology
3. Institute of Biochemistry and Biophysics (IBB), University of Tehran

Introduction: Pure polymeric materials to be used as biomaterials cannot be used for high-performance applications due to Their unfavorable properties. Therefore, modification of substrate surfaces is essential for many applications. In the meantime, polymer brushes can be used to modify the polymer substrate. Substrate modification by polymer brushes can affect surface properties such as biocompatibility, friction, adhesion, and wettability. Of course, this method also has disadvantages, such as weak strength. Polymeric substrate surface modification method can be divided into two methods: physical and chemical. Chemical bonding is more desirable than physical bonding due to its long-term chemical stability. chemical surface modification methods based on grafting are divided into three categories: graft to, graft from, and graft through. In the grafting method, pre-prepared polymers react with the substrate functional groups to form bonded polymer chains. In this approach, radical controlled methods, anionic, and other polymerization techniques can be used. In the grafting from the method, polymer chains propagate from surface-attached initiators. In this method, density can be controlled. The grafting through method is often based on monomer groups attached to the surface. In this method, the polymer chains first grow in solution and then propagate. This method can be one of the most powerful processes for surface modification, but there is still a lot of work to be done to clarify its mechanisms.

Methods: In this study, reviewing various articles on the importance of polymer brushes in the manufacture of polymer substrates for various medical applications such as medical implants, biosensors, surgical equipment, and health products, the most important and up-to-date information was collected and presented as a review article.

Results: Modified polymer substrates can have various applications in biomedical due to obtaining the desired properties, some of which are briefly mentioned below. Anti-fouling surfaces have numerous applications in various medical fields such as medical implants, biosensors, surgical equipment, and health products. Their other use is in platelet adhesion. Among the types of polymeric biomaterials, polytetrafluoroethylene (PTFE) has been one of the

emerging research centers due to its excellent mechanical properties and chemical stability under biological conditions. Polymer brushes are used in drug delivery to achieve site-specific and time-controlled drug delivery to increase the effectiveness of the drug and reduce its side effects. Their other application is in microbial adhesion and biocompatibility.

Conclusion: The history of using biomaterials goes back to the distant past. Their desirable properties such as non-toxicity, corrosion resistance, controlled degradability, and the like have made them suitable for biomedical applications, but achieving the desired mass properties requires its modification. Advances in recent decades have made these modified surfaces have many applications in biomedical.

Keywords: Polymer Brushes, Modified Biomaterials, Grafting, Drug Delivery, Anti-fouling Surfaces

Chitosan applications in studying and managing osteosarcoma (Review)

Parisa Maleki Dana,[1] Jamal Hallajzadeh ,[2,*] Zatollah Asemi,[3] Mohammad Ali Mansournia,[4] Bahman Yousefi,[5]

1. Research Center for Biochemistry and Nutrition in Metabolic Diseases, Institute for Basic Sciences, Kashan University of Medical Sciences, Kashan, Iran.
2. Department of Biochemistry and Nutrition, Research Center for Evidence-Based Health Management, Maragheh University of Medical Sciences, Maragheh, Iran.
3. Research Center for Biochemistry and Nutrition in Metabolic Diseases, Institute for Basic Sciences, Kashan University of Medical Sciences, Kashan, Iran.
4. Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.
5. Molecular Medicine Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

Introduction: Despite the low incidence of osteosarcoma in the general population, it has a high prevalence among adolescents. Due to the heterogeneity and complexity of osteosarcoma etiology, the underlying molecular processes involved in its pathology are not fully understood. Furthermore, the genotype of osteosarcoma can modify itself rapidly. Thus, targeted molecular methods are not as practical as desired. Osteosarcoma patients with a metastatic or recurrent form of the disease have shown an overall survival rate of 20% during the past 30 years and relapse rates of the disease are approximately 35%. While progressions in the field of osteosarcoma treatment are occurring slowly, conventional treatments of osteosarcoma are still not promising enough. Therefore, there is a need for developing novel therapeutic methods or enhancing currently available approaches. Chitosan is a linear polysaccharide composed of β--linked D-glucosamine and N-acetyl-D-glucosamine. This compound is derived from the deacetylation of chitin which is found in exoskeletons of insects and crustaceans as well as fungi cellular walls. Chitosan's features include but are not limited to low toxicity profile, ability to bind to nucleic acids, bio-adhesiveness, biocompatibility, biodegradability, and the capacity of permeabilization. These characteristics have made chitosan a proper candidate for pharmacological purposes.

Methods: Several in vitro and in vivo articles as well as pre-clinical and clinical trial studies have been gathered and reviewed from multiple databases such as PubMed, Scopus, and Google Scholar. In this review, we discuss the potential roles of chitosan in studying and treating osteosarcoma. We review the literature on chitosan's applications as a drug delivery system

and the possible benefits of chitosan in the field of bone tissue engineering and 3D culturing. Furthermore, the anti-cancer activities of different types of chitosan are reviewed.

Results: Chitosan-based formulations are shown to be useful for various purposes in osteosarcoma. The most common type of chitosan-based materials used in the osteosarcoma field are hydrogels, nanoparticles, and scaffolds. These formulations can be used as delivery systems of chemotherapeutic drugs (such as doxorubicin) and genes (e.g. PEDF and LacZ). Chitosan-based compounds are also able to exert anti-tumor effects, including apoptosis induction, inhibiting proliferation, and suppressing metastasis. In addition to the mentioned applications, chitosan-based compounds are useful for culturing different osteosarcoma cells lines which allows studying the pathogenesis of this cancer. Besides, they can be used in bone tissue engineering.

Conclusion: Based on the several studies conducted on the role of chitosan in the treatment of osteosarcoma, this polysaccharide provides a variety of beneficial effects in this field. Moreover, chitosan is an excellent option to use for studying osteosarcoma.

Keywords: Chitosan, osteosarcoma, delivery systems, tissue engineering, cell culture

Chronic sleep restriction outcome on the volumetric correlates, neuronal and glial number of the hypoglossal nucleus in a rat model (Research Paper)

Fatemeh Karimi,[1,*] Ali-Mohammad Kamali,[2] Ali Noorafshan,[3] Saied Karbalay-Doust,[4] Mohammad Nami,[5]

1. Histomorphometry and Stereology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
2. Department of Neuroscience, School of Advanced Medical Sciences and Technologies, Shiraz University of Medical Sciences, Shiraz, Iran
3. Histomorphometry and Stereology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
4. Histomorphometry and Stereology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
5. Department of Neuroscience, School of Advanced Medical Sciences and Technologies, Shiraz University of Medical Sciences, Shiraz, Iran

Introduction: Chronic sleep restriction (CSR) is known to result in various changes in brain structures including the dorsal respiratory nuclei of the brain stem. Obstructive sleep apnea has partly been resulted from reduced tone of the muscles including the tongue which are involved in maintaining airway patency during sleep. This study aimed at investigating whether CSR may result in structural changes in the hypoglossal nerve nuclei.

Methods: Three groups of male rats (each comprising 7) were randomly assigned to CSR, cage control and grid-floor control groups. CSR was imposed using the modified multi-platform box containing water for 18 hours/day for 21 days. At the end of 21 days, the rats' brain was removed and stained through the modified Giemsa method

Results: The total number of neuronal and glial cells did not show significant differences between the cage control and the other groups (p=0.3).

Conclusion: The current study provided evidence to support that CSR induced by the modified multiple platform approach for 18 hours/day over 21 days in rats, neither results in volume reduction, nor neuronal and glial cells loss in the hypoglossal nuclei in the brain stem.

Keywords: Sleep restriction, Stereology, Neuronal number, Hypoglossal Nuclei

Circular RNA - A possible connection between human cytomegalovirus and Gastric cancer (Review)

saman saeidi,[1] alireza mohebbi,[2,*] reyhane shaddel,[3]

1. golestan university of medical sciences(goums)
2. golestan university of medical sciences(goums)
3. golestan university of medical sciences(goums)

Introduction: Circular RNAs (circRNAs) are a type of single-stranded RNA formed as a covalently closed-loop by connection between the 3´ and 5´ ends unlike linear RNA form. It's a spectacular topic that still need more experiments so we can finally discriminate how important they are in humans. Unlike linear RNA, this type of noncoding RNA (ncRNA) is very stable in our bodies. CircRNA was first found in RNA viruses as early as the 1970s.by the functions that circRNAs have like micro RNA sponge, interaction with RNA binding protein(RBP) and regulatory effect on transcription and translation; It has been seen that circular RNAs can play role in many process such as signaling pathways, translation, cell cycle progression. Evidence suggest that circRNAs can be used as biomarker for caners. for example Hsa-circRNA-103809 Promotes Hepatocellular Carcinoma Development via MicroRNA-1270/PLAG1 Like Zinc Finger 2 Axis. given this information, we can focus on effect of circular RNAs on cancers. Cancer can occur due to direct or indirect effect of a microbe. several researches proved there is a bridge between cancers and viruses. These genomic ancient enemies of humans can play role in many aspects of living creatures. One of the substances that they can affect is circular RNA. since there is also connection between cancer and viruses, so why not trying to search about a possible path that viruses can use to cause cancers which is circular RNA pathway.in that case we used human cytomegalovirus relation with gastric cancer.

Methods: Systematic Review of published paper in data bases like PUBMED , Google scholar , NCBI and journals like journal of cancer.

Results: Human cytomegalovirus and circular RNAs: Clearly relation between viruses and circRNAs is strong even if they don't owned them. circSP100 shown to be increased during infection by HCMV and helped the infection itself. so viruses do use circRNAs for their own purposes directly. HCMV is the only beta herpes virus known to encode microRNAs that are involved in the regulation of diverse cell processes such as cell proliferation, apoptosis, differentiation, and carcinogenesis. It seems that we have new evidence of HCMV pathogenesis mediated by circRNAs pathways. they found that the host genes corresponding to the differentially expressed circRNAs were mainly involved in the regulation of host cell secretion pathways, cell cycle, and cell apoptosis, so since these RNAs are down/up regulated in HCMV

infection, they suggest that maybe circRNAs interact with HCMV DNA replication and latent infection. hsa_circ_0001445 and hsa_circ_0001206 are only two important circRNAs that can be used for diagnosis of HCMV infection among many others. these two are related to prostate cancer and also hsa_0001445 can be used for diagnosis of hepatocellular carcinoma (HCC). Gastric cancer and circular RNAs: Through each major function of circRNA, cancer can be the result. Previous studies have evaluated circRNAs as potential biomarkers for gastric cancer(GC). decrease in the circPVRL3 expression level is associated with the presence of GC. Circular RNA hsa_circ_0010882 promotes the progression of gastric cancer via regulation of the PI3K/Akt/mTOR signaling pathway. Human cytomegalovirus and Gastric cancer: Evidence suggest that HCMV is link to multiple human malignancies like gastric cancer. Human cytomegalovirus protein UL136 regulate IL6/STAT3 pathway, through down-regulation of miR-34c in GC cells. UL135 and 136 are risk factors associated with the development of gastric cancer. According to studies, an HCMV infection appeared to be significantly associated with an increased risk of GIC. The infection site resulting from this virus is within gastrointestinal tract. this connection was first mentioned in 1978.

Conclusion: so far we realized that gastric cancer can be related to HCMV and also circular RNAs. Also HCMV shown to have strong effect on many circular RNAs. Given all these information, we can understand the possibility of connection between GC and HCMV mediated by circular RNAs and this could be one of the pathways that this virus use. Many experiment needs to be performed in order to find this connection since there is so many circRNAs in our body. we think by following this path, we can achieve spectacular information about a new pathway that viruses can use against us and make this an opportunity for strike back to viruses.

Keywords: circRNA – Human cytomegalovirus(HCMV) – gastric cancer

Circular RNAs in tumorigenesis and cancer diagnosis (Review)

Zahra-sadat Mousavi,[1,*] Amir Atashi,[2] Roqaye Karimi,[3]

1. Student Research Committee, School of Allied Medical Sciences, Shahroud University of Medical Sciences, Shahroud, Iran
2. Stem Cell and Tissue Engineering Research Center, Shahroud University of Medical Sciences, Shahroud, Iran
3. Department of Hematology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran

Introduction: Cancer is a complex and common disease that has internal and external risks. The incidence and mortality rate of this disease is increasing every year and causes serious problems in world health and public health. For almost two decades, researchers have explored the role of non-coding RNA (ncRNA) in cancer biology. ncRNAs are stable in biological fluids and show tissue-specific expression. ncRNAs can act as biomarkers or key regulators of the cancer gene network. CircRNAs were first identified in viroids by Sanger et al. in 1976 and subsequently found in eukaryotes in 1979 by electron microscopy.

Methods: Circular RNAs (circRNAs) are non-coding RNAs that form a circular structure by covalent bonding and are resistant to exonuclease degradation due to the lack of 5′ cap and polyadenylated tails at the 3′ end. They are more stable than linear RNAs and have a longer half-life. CircRNAs are classified into three categories: intronic circRNAs (ciRNAs), exonic circRNAs (ecircRNAs), or exonic-intronic circRNAs (EIciRNAs).

Results: CircRNAs have several mechanisms of action: they can act as sponge miRNAs and prevent miRNA binding to mRNA and prevent mRNA degradation. They can act as protein sponges and prevent protein binding to mRNA. CircRNAs may act as local mediators for the transport of specific proteins from the cytoplasm to the nucleus and can also act as structural mediators, accumulating enzymes and substrates and influencing reaction kinetics. CircRNAs can act as transcriptional regulators to control host gene expression. Recent studies have shown that some circRNAs that contain the IRES or N6-methyladenosine (m6A) sequence can be translated into proteins. For example, circFBXW7 contains IRES sequences that can be translated into proteins. CircRNAs can be considered as new biomarkers due to their different expression in tissues and are associated with carcinogenesis and tumor progression by regulating cellular activity.

Conclusion: CircRNA has different mechanisms in human cancers, for example circAGFG1 increases expression in Triple-negative Breast Cancer

(TNBC), acts as a sponge microRNA for miR-195-5p, and causes TNBC cells to proliferate as well as tumor metastasis in vivo. CircDNMT1 increases expression in Breast Cancer (BRCA) and binds to P53 and AUF1 proteins, and the main mechanism of this circRNA is to increase Dnmt1 translation. CircSHPRH decreases in glioblastoma multiforme (GBM) and produces SHPRH, which suppresses tumors in human glioblastoma. A circRNA can play opposite roles in different cancers by acting as a sponge miRNA on several different mRNAs. For example, circHIPK3 targets miR-7 to enhance colon cancer growth and metastasis, It also targets miR-558 to suppress heparanase expression, which breaks down heparan sulfate chains in the extracellular matrix. Recently, the promising role of exosomal RNAs in cancer diagnosis have discovered. For example, circulating exosomal mRNAs were used to diagnose prostate cancer, and due to the different expression patterns between exosomal mRNAs and tissue mRNAs, urine circulating exosomal mRNAs are used as non-invasive biomarkers for prostate cancer diagnosis.

Keywords: CircRNA, Cancer, Tumorigenesis, Diagnosis, miRNA

Circulating inflammatory markers may mediate the relationship between low carbohydrate diet and circadian rhythm in overweight and obese women (Research Paper)

Atefeh Tavakoli,[1] Atieh Mirzababaei,[2] Forough Sajadi,[3] Khadijeh Mirzaei,[4,*]

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Introduction: Background: Low carbohydrate diet (LCD) can improve inflammation and obesity and also circadian rhythm disorders can lead to increased inflammation in obese individuals. The purpose of this study is to evaluate the association between adherence of LCD and circadian rhythm mediated by inflammatory markers including transforming growth factor-β (TGF-β), interleukin-1β (IL-1β) and Galectin-3 in overweight and obese women

Methods: 304 women affected by overweight and obesity were enrolled. We evaluated LCD scores by Semi-quantitative food frequency questionnaire (FFQ) of 147 items. The morning-evening questionnaire (MEQ) was applied to evaluate the circadian rhythm. Biochemical parameters such as inflammatory markers and anthropometric components were assessed.

Results: There was a negative significant correlation between adherence of LCD and circadian rhythm status. In other words, as the LCD scores increased, the odds of circadian rhythm disturbance in intermediate group and morning type persons decreased compared to evening type. It was showed that, IL-1β and Galectin-3 in intermediate and morning type groups, destroyed the significance of this relationship and may be considered as mediating markers.

Conclusion: Adherence of LCD can improve the circadian rhythm by reducing levels of inflammatory markers and may be considered as a treatment for obesity.

Keywords: low carbohydrate diet, circadian rhythm, inflammation, obesity

Class 1 integrons among Klebsiella pneumoniae isolated from urine samples of patients with urinary tract infections in Alborz province (Research Paper)

Leila Jabalameli,[1,*] Mahyar Rahmatpanah,[2] Hossein Gomar,[3] Mohammad Shokrgozar ashkar meidani,[4] Javad Jamali Pabandi,[5]

1. Department of Microbiology, Faculty of Sciences, Karaj Branch, Islamic Azad University, Karaj, Iran.
2. Department of Microbiology, Faculty of Sciences, Karaj Branch, Islamic Azad University, Karaj, Iran.
3. Department of Microbiology, Faculty of Sciences, Karaj Branch, Islamic Azad University, Karaj, Iran.
4. Department of Microbiology, Faculty of Sciences, Karaj Branch, Islamic Azad University, Karaj, Iran.
5. Department of Microbiology, Faculty of Sciences, Karaj Branch, Islamic Azad University, Karaj, Iran.

Introduction: Klebsiella pneumoniae (K. pneumoniae) is a Gram-negative opportunistic bacterium involved in community-acquired and nosocomial infections. Several infections such as pneumonia, liver abscess, meningitis, bloodstream infections, and urinary tract infections (UTIs) are caused by this bacterium, though it is found in normal flora of the mouth, skin and intestine. Different mechanisms and factors involved in the development and spread of antibiotic resistance. Among them acquisition of resistance genes especially via mobile genetic elements such as integrons is considered as the main factor in the wide distribution of antimicrobial resistance. In the present study, isolation of K. pneumoniae from urine samples and evaluating the presence of class 1 integrons among isolates were investigated.

Methods: The obtained isolated bacteria were confirmed as K. pneumoniae via inoculating in to MacConkey agar plates, gram staining, and biochemical tests such as oxidase, urease, SIM, TSI, OF, MR, and VP tests. DNA was extracted by boiling method and in order to amplify class 1 integrons, specific primers with the following sequences were used in PCR technique; hep58, 5’ TCATGGCTTGTTATGACTGT 3’ and hep59, 5’ GTAGGGCTTATTATGCACGC 3’.

Results: 80 K. pneumoniae were isolated from the urine samples of attendees with UTI. 35 (43.75%) isolates were obtained from males and the rest of the samples were isolated from females. No significant difference was observed in different age ranges of attendees. 29 isolates were positive in terms of class 1 integrons. PCR amplification of these genes showed five diverse bands of 2.1, 1.9, 1.1, 0.85, and 0.5 kb.

Conclusion: Knowing about the increase in Klebsiella pneumoniae isolates harboring class 1 integrons, involved in dissemination of resistant isolates among population, may help physicians control the spread of infections and also choose the more effective therapies.

Keywords: Klebsiella pneumoniae, urinary tract infections, class 1 integrons, PCR

Classical Enterotoxin Genes Investigation of Staphylococcus aureus Isolated from Urine Clinical Sample using Molecular Technique
(Research Paper)

Ghazale Faridfar,[1] Mohammadreza Akbari,[2,*] Shahin Faridfar,[3] Amin Nourian,[4]

1. Islamic Azad University, Tehran Medical Sciences Branch, Faculty of Sciences & Technology, Tehran, Iran.
2. Biology Science and Technology Center, Faculty and Research Institute of Basic Science, Imam Hossein Comprehensive University, Tehran, Iran
3. Biology Science and Technology Center, Faculty and Research Institute of Basic Science, Imam Hossein Comprehensive University, Tehran, Iran
4. Biology Science and Technology Center, Faculty and Research Institute of Basic Science, Imam Hossein Comprehensive University, Tehran, Iran

Introduction: Staphylococcus aureus is an important pathogen of humans in nosocomial and non-nosocomial infections. These bacteria can produce several extracellular toxins. Staphylococcal enterotoxins (SEs) are the common notable virulence factors in these bacteria. Classical SEs classified into 5 serological types (SEA to SEE) based on their antigenicity. The genes encoding the enterotoxins are often on a variety of distinct mobile genetic elements. Hence, the distribution of enterotoxins can vary broadly among various S. aureus isolates. Accordingly, an annual-long update of data on the prevalence of S. aureus and its enterotoxins (SEs) genes improves the analysis, prevention, and treatment plans in every region. So, the presence of enterotoxin genes in S. aureus strains isolated was evaluated from the clinical sample by the molecular technique.

Methods: In this study, we analyzed random urine samples obtained from clinical specimens for tracking of S. aureus strains through the traditional procedure. Next, isolates were evaluated for the presence of toxin-producing genes (A-E) using Polymerase Chain Reaction (PCR) assay. Finally, the highest frequencies of isolates containing classical enterotoxin gene (SEs) were reported.

Results: In this scheme, a total of 50clinical urine samples suspected of staphylococcus were elected, which the S. aureus was confirmed utilizing the conventional method in 36 of them. Following bacteriological methods, 36 isolates were gram-positive and beta-hemolytic. The effect of the mannitol salt agar, catalase, and tube coagulase assays was also approved for them. The results of the molecular technique demonstrated 17 cases were positive only for one type of SEs (SEA) while the remaining samples were negative. None of the isolates were also positive for SEs (B, C, D, E). Consequently, the results showed the meaningful presence of the genes encoding staphylococcal enterotoxin A (SEA) in most isolated strains.

Conclusion: The outcome of this study revealed that most S. aureus strains isolated from urine samples produced SEA compared to other SEs. This means most presumably of the staphylococcal strains approved using the PCR technique were enterotoxigenic. We found probable evidence that the SEA gene plays an important part in infectious staphylococcal genomes. Accordingly, the relatively high prevalence of the enterotoxins A(SEA) gene in the isolates indicated the potential of these bacteria to cause urinary infection. In general, information from this study has provided a reliable understanding of S. aureus spread in the clinical infection diseases that reflects the current poor control of these bacteria.

Keywords: Classical Enterotoxin; Polymerase Chain Reaction; Staphylococcus aureus; Enterotoxin A.

Cloning of a novel designed guide RNA into the CRISPR/Cas9 vector for knocking out HPV16 E6 oncogene (Research Paper)

Niloofar Khairkhah,[1] Azam Bolhassani,[2,*] Reza Najafipour,[3]

1. Department of Molecular Medicine, School of Medicine, Qazvin University of Medical Sciences, Qazvin, Iran
2. Department of Hepatitis and AIDS, Pasteur Institute of Iran, Tehran, Iran
3. Genetics Research Center, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran

Introduction: Human papillomavirus (HPV) is the most common sexually transmitted virus in the world. About 70% of cervical cancers are caused by the most oncogenic HPV genotypes of 16 and 18. Since available prophylactic vaccines do not induce immunity in those with established HPV infections, the development of a therapeutic approach remains essential. CRISPR/Cas9 system is a genome-editing method that can be considered as a therapeutic approach by knocking out the viral oncogenes resulting in tumor growth suppression. In this study, we aimed to clone a novel designed guide RNA into the PX330 CRISPR/Cas9 all-in-one vector since this part of the study is considered a significant bottleneck.

Methods: PX330 all-in-one CRISPR/Cas9 vector had been purchased from Zhang's lab. E6 Target site of HPV16 were selected by utilizing CHOPCHOP online tool. one single-stranded oligo was ordered in the form of incompatible overhang for correct orientation and cloned into the plasmid using BbsI restriction enzyme. The final confirmation of the cloned guide RNA oligo was conducted by Sanger sequencing.

Results: The final confirmation by Sanger sequencing showed that the designed oligo was successfully cloned into the px330 all-in-one CRISPR/Cas9 vector.

Conclusion: The CRISPR/Cas9 system has demonstrated high-fidelity gene editing and has become widely used for specific targeting and cleavage. This is a viable route of treatment that could supplement or potentially replace the current treatments of surgery, chemo and radiation therapy.

Keywords: human papillomavirus; cervical cancer; CRISPR/Cas9

Coagulopathy in COVID-19 Patients and Endovascular Treatment, Reports of 4 Patients (Research Paper)

Erfan Mohammadi-Vajari,[1,*] Mohammad-Ali Mohammadi-Vajari,[2] Mohammadreza Babaei,[3]

1. Student of Medicine, Faculty of Medicine, Guilan University of Medical Sciences, Rasht, I. R. Iran
2. Department of Radiology, Faculty of Medicine, Iran University of Medical Sciences, Tehran, I. R. Iran
3. Department of Radiology, Firouzgar Hospital, Iran University of Medical Sciences, Tehran, Iran

Introduction: Due to the respiratory infection of SARS-CoV-2, COVID-19 pandemic has now become a global threat . Numerous papers have addressed the pulmonary symptoms of this disease which highly contributed to the identification of the pathogenesis of COVID-19 infection. It seems that ACE2 receptors are involved in the entrance of the virus into the cells. Regarding the presence of these receptors on the surface of the alveoli epithelial cells and vascular endothelium, these cells and organs are prone to this virus . The incidence of thrombotic complications such as Pulmonary Thromboembolism, deep vein thrombosis, ischemic stroke, cardiac infarction, and arterial embolism is high in COVID-19 patients which has been reported in numerous studies before . The initial clinical sign of coagulopathy in COVID-19 is organ failure while hemorrhagic complications are less common. The changes in the hemostatic markers such as D-dimer and fibrin and fibrinogen products have indicated that the basis of the coagulopathy is probably the fibrin products . However, the hemorrhagic complications of COVID-19 patients have received less attention. In this context, the current study presents four COVID-19 patients with hemorrhagic complications and describes their treatments.

Methods: In this article, 4 cases of COVID-19 patients with hemorrhagic complications are presented. All 4 patients were hospitalized in ICU and received routine COVID-19 treatments such as heparin prophylaxis. During hospitalization, all four patients had rectus sheath hematoma and retroperitoneal hemorrhage. For controlling which, they underwent embolization. Embolization of the inferior epigastric artery and the anterior trunk of internal iliac artery was carried out under fluoroscopy-guided angiography. The active hemorrhage of the patients was controlled.

Results: Three patients recovered after the treatment and were discharged while one patient, unfortunately, died due to the severity of the pulmonary involvement, old age, and hemorrhage. First, the hemorrhage of these patients was considered to be the result of the hemorrhagic complications due

to the use of heparin. But the hemorrhage volume was not justifiable with the symptoms and complications of prophylaxis dosage of heparin. The attention was gradually drawn to the coagulopathy of the COVID-19 patients. Further investigations are required to clarify the role of effective factors and complications of coagulopathy in patients with COVID-19 and their appropriate treatment.

Conclusion: There is increasing awareness of coagulation disorders in Covid-19 infection. Thrombotic complications seem to be common among this patient population, which may necessitate preparing appropriate guidelines for its management. However hemorrhagic complications and their proper treatment should also be taken into consideration in covid-19 infection .

Keywords: Blood coagulation disorders, COVID-19, SARS-CoV-2, Interventional radiology

Cognition and microbes; emerging a new era in Neuroscience (Review)

Soroush Fazel,[1,*] Fatemeh Yousef Saber,[2]

1. Department of Cognitive Neuroscience, Faculty of Education and Psychology, University of Tabriz, Tabriz, Iran
2. Department of Cell and Molecular Biology and Microbiology, Faculty of Biological Science and Technology, University of Isfahan, Isfahan, Iran

Introduction: Each human body has a unique microbial signature consisting of approximately ten trillion microbes (mainly bacteria; Actinobacteria, Bacteroidetes, Firmicutes, Proteobacteria, etc.) that strongly affect all aspects of their physiology, pathology, and even cognition. Several studies have indicated the evolutionary role of microbial composition and complexity in human brain development, behavior regulation, and cognitive functions such as sociability. However, neural pathways and neurotransmitters could strongly affect the microbiota dynamics as well.

Methods: This article is a brief review on how the human microbiome could affect various cognitive processes as well as cause/controlling different diseases and behaviors. Google Scholar and Pubmed databases were used to gather this information using these keywords: microbiota, cognitive neuroscience, cognitive disorders, and gut-brain axis.

Results: It has been documented that there are numerous bidirectional associations between the brain and human microbiome, especially gut microbiota which could be divided into 4 main categories: i) The vague nerve and central lymphatic vessels, ii) the hypothalamic-pituitary-adrenal axis (HPA), iii) the immune system and its cytokines, iv) essential metabolisms like Tryptophan–Kynurenine and short-chain fatty acids. These communications could result in both regulating behaviors and causing diseases which could be discussed as follows: Aside from the effect of bacterial genes and metabolites on different levels of brain structure and function, they also participate in a wide range of cognitive processes such as memory and learning. Recent studies have reported other behavior-related impacts of microbiota like social behavior, intimate relationship, sexual behavior, mate selection, and maternal care. On the other hand, simultaneous gut microbiota colonization and cognitive development occur right after childbirth. Conducting different experimental methods namely germ-free studies, antibiotic administration, assessing probiotic effects and microbial transplant confirmed the crucial role of bacteria in causing major cognitive deficits. Addiction to alcohol, opiates, and psychostimulants, eating disorders, depression, anxiety, and stress, autism, and schizophrenia are just a few approved examples.

Conclusion: Microbiome-brain association has attracted significant attention in the past decade. The implication of this system could be a turning point in characterization and more importantly in the treatment of severe psychiatric disorders by altering microbial population using probiotics, prebiotics, or other natural compounds.

Keywords: Microbiota, Cognitive neuroscience, Cognitive disorders, Gut-brain axis

Coinfections in SARS-CoV-2 pateints with other Respiratory viruses (Review)

Seyed Amir Mohammad Seyed Mirzajani,[1] Seyed Reza Mohebbi,[2,*] Seyed Masoud Hosseini,[3] Piruz Shadbash,[4] Mahsa Saeedi Niasar,[5] Hamid Asadzadeh-Aghdaei,[6]

1. Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences
2. Research Center for Gastroenterology and Liver Diseases, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
4. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
5. Research Center for Gastroenterology and Liver Diseases, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
6. Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Introduction: In December 2019, a series of unknown viral pneumonia cases later named coronavirus disease 2019 (COVID-19) or SARS-CoV-2 was reported in Wuhan, China. The virus spread rapidly beyond Wuhan, affecting numerous nations, regions, and territories worldwide and infecting over 219 million people to date (24 September 2021). As a result, COVID-19 has become a worldwide concern and a public health issue. Coronavirus is transmitted mostly by respiratory droplets spread into the air after coughing or sneezing. Coronavirus usually leads to fever, tiredness, dry cough, myalgia, and shortness of breath but the disease has a large variety of symptoms that make it difficult to diagnose accurately. Symptoms such as runny nose, sore throat, diarrhea, headache, conjunctivitis, loss of taste or smell, dizziness, loss of appetite, and nausea have also been reported in some patients. Organ failures, such as acute respiratory distress syndrome and even death, may be likely in severe cases.

Methods: Coinfection rates between SARS-CoV-2 and other respiratory viruses have been reported in some studies. Co-infection with SARS-CoV-2 and other respiratory viruses has been observed in several reports from the United States, China, and Iran. Influenza virus, respiratory syncytial virus, metapneumovirus, adenovirus, parainfluenza virus, rhinovirus/enterovirus,

human bocavirus, and non-SARS-CoV-2 coronavirus are those which have been seen in these reports.

Results: Coinfections with Respiratory viruses in COVID-19 patients are often demonstrated and may lead to higher morbidity and death rates. During a SARS-CoV-2 infection, the pulmonary structure is significantly damaged, similar to influenza virus pneumonia. The assault of virus in alveolar epithelium and bronchial mucosa, the destruction of the epithelium, and enormous effusion in the bronchiole lumens of the infected individuals have all been reported in autopsy studies. These pathologic results might explain why COVID-19 patients are more likely to get infected with common respiratory infections, as some previous clinical trials and postmortem reports have shown. According to the findings of investigations done on co-infected individuals with COVID-19 and other respiratory viruses, several clinical and laboratory findings were similar in both illnesses, that makes it challenging to diagnose these co-infected patients properly.

Conclusion: Differentiating other causes of respiratory disease from COVID-19 during a COVID-19 pandemic is difficult since COVID-19's clinical signs are similar to those of other respiratory viruses. It shows that monitoring for co-infection with different types of respiratory viruses in patients with certain conditions should be properly considered to choose the right treatment strategies and effective management for COVID-19 patients. SARS-CoV-2 may also be underdiagnosed due to false-negative results for co-infection with other viral respiratory diseases, according to some studies. To enhance clinical management decisions and results, it is proposed that wider viral evaluations be done.

Keywords: SARS-CoV 2, Co-infection, COVID-19, Coronavirus, Respiratory viruses

Colorectal Cancer and COVID-19 (Review)

Javad Yaghmoorian Khojini,[1] Ali Osmay Gure,[2,*]

1. Department of Medical Biotechnology, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
2. Department of Medical Biology, Acibadem University, Istanbul, Turkey

Introduction: An outbreak of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), has rapidly spread from Wuhan, China for the first time. The number of people infected with Covid-19 caused by the new coronavirus in the world has reached 186 million people so far and the death of 4 million people has been confirmed due to the disease. Colorectal cancer is one of the leading causes of death worldwide and is one of the most common gastrointestinal malignancies, the underlying cause of which is not exactly known. In this study, we will discuss the results presented by some studies on the effects of COVID-19 on hospital admissions and other cases of colorectal cancer patients.

Methods: This review study was done using various update articles, books and authoritative scientific sites.

Results: Coronavirus disease 2019 (COVID-19), a rapidly evolving pandemic infecting more than 180 million people worldwide according to the World Health Organization (WHO) to date. Colorectal cancer (CRC) is one of the leading causes of death worldwide. It is the fourth most common cancer in the world in terms of mortality after lung and breast cancer, ranking third among women and among men after lung and prostate cancer. Patients with cancer might be at an increased risk of infection with COVID-19. According to one Meta-analysis study the prevalence of COVID-19 infection in CRC patients was 45.1% in the global population. In a 2020 study in Shanghai, 710 patients with colorectal cancer, the rate of surgery during the COVID-19 epidemic increased by about 15 percent and the average length of hospital stay in these patients increased significantly. In a study conducted in France in 2020 compared to 2019, there was a decrease in the admission and surgery of patients with colorectal cancer, and this amount varied between 10 and 30%. In a study in the UK, this declining trend was much greater in 2020, with a reduction of between 30 and 80% in the admissions and surgeries of patients with colorectal cancer compared to the same time last year. In a study in Italy in 2020, the number of selective colonoscopies decreased sharply but the rate of detected cancer as well as high-risk adenomas increased. A recent study of 73 hospitalized patients with COVID-19 demonstrated that the feces of approximately 53.42% of these patients was positive for SARS-CoV-2 RNA. This finding concurred with the other rates published by Wang et al (20.5%),

Lee et al (19%) and Yang et al (14%) demonstrating that gastrointestinal and colorectal cancer was one of the most common malignancies among patients with cancer who contracted COVID-19.

Conclusion: This study shows that the trend of hospital admissions of patients with colorectal cancer during the COVID-19 epidemic in the world is not a steady trend and in some countries such as China this trend is increasing and in some countries such as Britain and France has been declining. It is generally recommended to increase health care and appropriate treatment process during the COVID-19 epidemic for cancer patients, especially colorectal cancer.

Keywords: COVID-19, CRC, hospital admissions, trend, treatment

Colorimetric PCR-based detection of a bacterial cause of urinary tract infection (Research Paper)

Shahrzad Salmanian,[1] Hamidreza Mollasalehi ,[2,*]

1. Department of Cellular and Molecular Biology, Faculty of Modern Science and Technology, Islamic Azad University, Medical Sciences Branch, Tehran, Iran
2. Department of Microbiology and Microbial Biotechnology, Faculty of Biological Sciences and Technology, Shahid Beheshti University, Tehran, Iran

Introduction: Nosocomial infections such as urogenital and urinary tract infections are caused by opportunistic bacteria namely, Morganella morganii. Therefore, a rapid and specific molecular detection method is needed for early diagnosis of the agent for accurate therapy. In this study, a visual colorimetric PCR detection assay was developed using a metal indicator for M. morganii.

Methods: The bacterial cells were cultured overnight to reach the log phase in their growth curve, followed by genomic DNA extraction. After analyzing the quality and quantity of the extracted DNA using spectroscopy, the target gene of M. morganii was amplified by an optimized PCR protocol using designed primers. Furthermore, the specificity of the assay was assessed using a mixture of eight gram-negative bacteria (Shigella boydii, Yersinia enterocolitica, Citrobacter freundii, Klebsiella pneumonia, Enterobacter aerogenes, Pseudomonas aeruginosa, Burkholderia cepacia, Serratia marcescens) with and without the target bacteria (M. morganii). Finally, the amplification PCR products were investigated by the metal indicator, hydroxy naphthol blue (HNB) dye which was added to PCR amplicons in an endpoint approach. The limit of detection (LOD) was investigated by a decimal dilution of the extracted DNA.

Results: The quantity of the M. morganii extracted nucleic acid was measured to be 101 µg mL-1, which was appropriate for further experimental analysis. The color change of dark blue to light blue was observed in the positive sample including M. morganii but not in the negative sample without M. morganii. Furthermore, the limit of detection (LOD) of the assay was visualized up to a second dilution tube. This value was determined to be 1.01 µg mL-1 of the amplified genomic DNA of M. morganii by HNB indicator.

Conclusion: The optimized conventional PCR method with the instrument-free colorimetric detection could be an efficient and simple detection technique for rapid M. morganii identification, especially in urinary tract infections.

Keywords: Morganella morganii; PCR; microbial detection; colorimetric identification; molecular diagnosis

Commercial products in the field of biotechnology (Review)

Zahra Abpeikar,[1] Ehsan Bakhshian-Dehkordi,[2] Mohsen Safaei,[3,*]

1.
2.
3. Department of Medical Biotechnology, School of Advanced Technologies, Shahrekord University of Medical Sciences, Shahrekord, Iran

Introduction: Introduction: The application of biotechnology in the 21st century is so great that it has dramatically affected the economy, health, treatment, environment, education, agriculture, industry, nutrition, and other aspects of human life. One of the most complex stages of new technologies in biotechnology products is the transfer stage Research findings into the production field, which is referred to as --technology transfer from research to production- or -commercialization-. Many commercial products are produced on a large scale by microorganisms or various approaches, leading to extensive developments in biotechnology.

Methods: Methods: This review was prepared via searching the databases of Science Direct, Directory of Open Access Journals (DOAJ), Google Scholar, Pub-Med (NLM), Scopus, Web of Science, and hand searching using relative keywords.

Results: Results: The commercial applications of biotechnology will be found in several industrial sectors, including pharmaceuticals, chemicals, antibiotics, enzymes, products from genetically engineered microorganisms, transgenic eukaryotes, nanodeliverables, enterprising artificial intelligence, synthetic biology, etc. Modern drug discovery relies heavily on computer modeling of drug-target interactions. However, in the past, and to a more limited extent today, laboratory screening programs are the route to discovering new antibiotics; however, using bioinformatics methods compared to traditional methods to design new drugs or antibiotics can save a lot of cast and time. Another important approach in the commercialization of biotechnology products is genetic engineering methods such as genetically engineered human proteins. To produce somatotropin as a human protein, the mRNA for bovine somatotropin (BST) is obtained from an animal. Then, the mRNA is converted to cDNA by reverse transcriptase. The cDNA version of the somatotropin gene is then cloned into a bacterial expression vector with a bacterial promoter and ribosome-binding site (RBS). The construct is transformed into Escherichia coli, and recombinant bovine somatotropin (rBST) is produced. Milk production increases in cows treated with rBST. Nanodimensional materials are currently being actively researched in biomedical sciences to develop better therapies, imaging modalities, and in some cases, a combination of both known as theranostics. Based on the

source materials, these nanoparticulate systems can be classified as (a) lipid nanomaterials, (b) polymeric nanomaterials, (c) inorganic nanomaterials, (d) carbon nanomaterials, (e) biomimetic nanomaterials, and (f) peptide nanostructures. Due to the importance of nanoparticles such as nanoliposomes in the production of mRNA-based vaccines, including the COVID-19 vaccine, recently, it has received a lot of attention. In the recent digital era, biotechnology has also expanded its wings to develop sophisticated, intelligent devices. Points of care (POC) devices result from collaboration between biotechnology, biochemistry, electronics and marketing. Major applications of POC devices are the test kits available in the market to detect many clinical conditions. POC devices are equally growing their business in both the developed and developing world. In 2011, POC testing devices shared a significant market of approximately $15 billion in total $51 billion markets of the total in vitro diagnostics, which signifies the fast pace commercialized growth of these systems. This commercial share is expected to increase with a 4% annual growth rate. The USA, Europe and Asia cover the top consumers of the point of care devices. In the last two decades, due to the importance of biotechnology drugs and their very effective role in the treatment of many diseases, the process of commercialization and sales of these products has grown significantly in the world and many large companies have made huge economic gains for themselves and their country by investing in this field. The United States is the largest investor in the research, production, and sales of biotechnology pharmaceutical products; therefore, investigating the market of biotechnology drugs can provide an overview of the commercialization process and sales market of this type of drugs in the world.

Conclusion: Conclusion: Market research and sales trend of each of the industrial biotechnology products including drug groups (monoclonal antibodies, cytokines, growth factors, blood factors, recombinant hormones, protein fusion and recombinant enzymes) or other products in the field of chemicals, antibiotics, artificial intelligence, nanotechnology and etc. is necessary for interested researchers in the field of commercialization of biotechnology products.

Keywords: Keywords: Biotechnology, Commercialization, Industrial products, Pharmaceuticals

Comparative inflammatory cytokines gene expression in culture of human macrophages infected with Leishmania tropica and L. major parasites (Research Paper)

Fatemeh Darzi,[1,*] Mahmoud Nateghi Rostami,[2] Roshanak Davoudian,[3]

1. Department of Parasitology, Pasteur Institute of Iran
2. Department of Parasitology, Pasteur Institute of Iran
3. Department of Parasitology, Pasteur Institute of Iran

Introduction: Human cutaneous leishmaniasis is mainly caused by two species Leishmania tropica and L. major in Old World. The type of skin lesion, its duration, severity and appearance is different between Anthroponotic Cutaneous Leishmaniasis (ACL) due to L. tropica and Zoonotic CL (ZCL) due to L. major. Since Pro- and anti-inflammatory cytokines significantly contribute in severity and outcome of CL lesion, this experiment aimed to compare the gene expression changes of these cytokines in culture of human macrophages infected with L. major and L. tropica parasites.

Methods: Peripheral blood mononuclear cells were isolated from a healthy individual without the history of CL from non-endemic region and macrophages were prepared by culture of adherent monocytes in 6well flat-bottomed plates for 6 days in 37 °C incubator with 5% CO2. Macrophages (3x10^5/well) were stimulated with either live L. major or live L. tropica promastigotes (Parasite:MQ ratio of 10:1) or unstimulated. At three time points T1=4, T2=10 and T3=24 hours after stimulation, RNAs were extracted and gene expression of TNF, IL-1B, IL- 6, TGF-B, and IL-10 were measured by relative real-time RT-PCR method using ΔΔCt calculation.

Results: Significant upregulation of TNF, TGF-B and IL-1B genes was shown in stimulated macrophages. The expression of IL-1B in macrophages stimulated with L. major was significantly higher than that of L.tropica. In L. tropica stimulated macrophages the expression of TNF was 93.05 fold higher in T2=10 hr compared to T1=4 hr and significantly decreased after 24 hr. In L. major stimulated macrophages the expression of TGF-B was 213.78 fold higher in T2=10 hr compared to T1=4 and significantly decreased after 24 hr, but in L. tropica stimulated macrophages TGF-B expression was significantly higher in T3=24 hr culture.

Conclusion: This study suggested alterations in pro-inflammatory cytokine IL1B and anti-inflammatory cytokine TGF-B associated with L. major vs. L. tropica infection in vitro. Changes in pro-pro- and anti-inflammatory cytokines seems to play a role in differences occur between severity/appearance of ACL and ZCL lesions.

Keywords: Leishmania; Inflammatory cytokines; Macrophage; Cutaneous leishmaniasis; Immunology

Comparing the Effects of Methanol Extract of Ficcus carica and Spirulina platensis with Silybum marianum on Liver Tissues in the Model of Fatty Liver Induced by Carbon Tetrachloride of Cyprinus carpio (Research Paper)

Tahereh Naji,[1,*] Homayoun Hosseinzadeh,[2] Shahrbanoo Nobakht Sarokalaei,[3] Ziba Kolouei,[4]

1. Department of Basic Sciences, Faculty of Pharmacy and Pharmaceutical Sciences, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.
2. Iranian Fisheries Science Research Institute, Agricultural Research and Education Organization, Tehran, Iran
3. Department of Basic Sciences, Faculty of Pharmacy and Pharmaceutical Sciences, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.
4. Department of Basic Sciences, Faculty of Pharmacy and Pharmaceutical Sciences, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.

Introduction: The use of natural plant-based substances in the treatment of liver disease in traditional medicine has a long history. Liver is the most common place for toxin accumulation and one of these toxin is carbon tetrachloride . Many industrial and natural compounds are used to reduce its toxicity. Ficcus carica are one of the most important medicinal plants for the treatment of liver disorders. Spirulina platensis is a water-soluble microalgae with many nutritional properties, including antioxidant, anti-inflammatory and fat-reducing properties. Silybum marianum is an antioxidant and liver-protecting compound that stabilizes the plasma membrane of the liver cell.

Methods: The purpose of this study was to compare the effects of methanol extract of Ficcus carica and Spirulina platensis with Silybum marianum on liver tissues in the model of fatty liver induced by carbon tetrachloride of Cyprinus carpio. In this study, 100 male and female Cyprinus carpio, with 15±5 gr weight, were divided into 10 unequally sized groups. There were four control groups, control 1 was intact, control 2 olive oil, control 3 carbon tetrachloride diluted with olive oil at a ratio of 3:1 and the other groups was injected into the muscle between dorsal fin and lateral line of fish with a dose of 1ml / kg of fish weight in the remaining 6 aquariums. After 24 hours from injection, doses of 100 and 200 ml / kg of fish weight from each extracts were injected into treatment groups. This was repeated 6 times every 48 hours. Tissue samples were taken from liver, and hematoxyline eosin staining was performed.

Results: The results showed histopathological studies in the case group of carbon tetrachloride compared to the control group. Histological results of liver in fishes showed that effect of carbon tetrachloride toxicity on liver tissue were cell degeneration, increase of fat cells and lysis of hepatocyte

Conclusion: Treatment with Ficcus carica and Spirolina platensis extract showed a positive effect of extracts on the improvement of liver lesions, but the effect of Silybum marianum on the improvement of lesions was more prominent.

Keywords: Toxicity, Silybum marianum, Ficcus carica, Spirulina platensis, Cyprinus carpio

Comparing the Effects of Methanol Extract of Ficcus caricaand Spirulina platensis with Silybum marianum on Liver enzymes and Hematological factors in the Model of Fatty Liver Induced by Carbon Tetrachloride of Cyprinus carpio (Research Paper)

Tahereh Naji,[1,*] Homayoun Hosseinzadeh,[2] Shahrbanoo Nobakht Sarokalaei,[3] Ziba Kolouei,[4]

1. Department of Basic Sciences, Faculty of Pharmacy and Pharmaceutical Sciences, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.
2. Iranian Fisheries Science Research Institute, Agricultural Research and Education Organization, Tehran, Iran
3. Department of Basic Sciences, Faculty of Pharmacy and Pharmaceutical Sciences, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.
4. Department of Basic Sciences, Faculty of Pharmacy and Pharmaceutical Sciences, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.

Introduction: Fatty liver in medicine is a reversible condition of the accumulation of fat vacuoles in the liver cells, which is characterized by liver inflammation. The main causes of fatty liver in Iran are diabetes, obesity, malnutrition and sudden weight loss. Defects in blood factors can cause many problems, including weakness, lack of concentration, hot flashes, increased risk of infection, shortness of breath, depression, insomnia, and decreased sex. Fatty liver disease is diagnosed by elevated liver enzymes.

Methods: In this study, 100 male and female Cyprinus carpio, with 15±5 gr weight, were divided into 10 unequally sized groups. There were four control groups, control 1 was intact, control 2 olive oil, control 3 carbon tetrachloride diluted with olive oil at a ratio of 3:1 and six treatment groups was injected into the muscle between dorsal fin and lateral line of fish with a dose of 1ml / kg of fish weight in the remaining 6 aquariums. After 24 hours from injection, doses of 100 and 200 ml / kg of fish weight from each extracts were injected into treatment groups. This was repeated 6 times every 48 hours. Then, blood samples were collected from caudal fin to measure liver enzymes (ALP, AST, and ALT), TG and cholesterol. Data were analyzed by SPSS. The standard deviation turned out to be significant (P≤0.05).

Results: The results showed a remarkable increase in liver enzymes and TG as well as cholesterol and histopathological studies in the case group of carbon tetrachloride compared to the control group. After the injection of extracts, a significant decrease (p≤0.05) was observed in the liver enzymes and triglyceride and cholesterol levels. The greatest effect in reducing liver enzymes, cholesterol and triglycerides was related to Silybum marianum at a dose of 200 mg / kg

Conclusion: The Ficcus carica extract and Spirulina platensis in many cases are close to Silybum marianum, which shows the importance of their effect in the treatment and prevention of fatty liver. Regarding blood factors, the greatest effect in treating the toxic effects of carbon tetrachloride is related to fig extract, then Silybum marianum and then Spirulina platensis

Keywords: Liver enzymes, Silybum marianum, Ficcus carica, Spirulina platensis, Cyprinus carpio

Comparing the Effects of Oleoresin of Pistacia Atlantica (Saqez) Tree and Diclofenac gel in Improving the Knee Osteoarthritis (Research Paper)

Hesam Adin Atashi,[1,*]

1. Young Researchers and Elite Club, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

Introduction: Osteoarthritis is the most common chronic rheumatoid disease, which affects the cartilage and tissues around the joints. This disease is one of the main causes of the pain and disability among older adults in most countries of the world. This disease does not have definitive treatment, and the used treatment controls the symptoms and pain. Turpentine can inhibit many of the enzymes involved in the inflammation process of osteoarthritis disease. Formulation of turpentine cream was used to reduce the pain, inflammation, and problems of patients with knee osteoarthritis with the aim of reducing the serious side effects of conventional therapies.

Methods: Clinical effects of this formulation on 84 patients with knee osteoarthritis (grade 2 and 3) were evaluated in a double-blind clinical trial study for three months, and diclofenac gel was used as a control drug. The mentioned formulation was analyzed for standardization with the GC-Mass apparatus. A WOMAC international questionnaire was used to assess the therapeutic trend. Results were analyzed by using SPSS 19 software

Results: According to the results, the improvement trend was observed in both groups, while the percentage of improvement in the symptoms of the disease was significantly higher in the turpentine group than that in diclofenac gel group ($P<0.05$).

Conclusion: According to the studies performed, the turpentine cream significantly reduces the pain and stiffness of patients' joints in performing the daily tasks. It is one of the most common problems of this disease

Keywords: Osteoarthritis, Turpentine, Diclofenac, WOMAC questionnaire

Comparison and optimization of detection methods for enveloped virus in vegetables (Research Paper)

Maedeh Rafieepoor,[1] Seyed Reza Mohebbi,[2,*] Seyed Masoud Hosseini,[3] Mohammad Tanhaei,[4] Mahsa Saeedi Niasar,[5] Hamid AsadzadehAghdaei,[6]

1. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
2. Research Center for Gastroenterology and Liver Diseases, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
4. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
5. Research Center for Gastroenterology and Liver Diseases, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
6. Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Introduction: Studies around the world show that many gastrointestinal outbreaks in communities are caused by the consumption of fruits and vegetables contaminated with enteric viruses such as Noroviruses, HAV, HEV, Sapovirus and etc. Limited methods have been reported for enteric virus detection from the surface of vegetables, however they usually showed a low viral recovery rate. These techniques have also been limited to non-envelop viruses. Recently, with regard to the prevalence of SARS-CoV-2, and the observation of some gastrointestinal complications such as diarrhea, vomiting, etc. in patients with Covid-19, it is necessary to develop and evaluate the concentration methods for enveloped viruses. The present study was performed to investigate and optimize the current methods for concentrating and detecting enveloped viruses.

Methods: To investigate and optimize a method for detecting enveloped viruses, two concentrations of TGBE and PEG were used to precipitate the viral particles. In this survey, a model virus called avian infected bronchitis (IBV) was used to evaluate the recovery percentage. A certain amount of IBV was inoculated into the lettuce leaf sample and its recovery was quantitatively calculated by a specific primer set that was designed based on SYBR GREEN RT-qPCR assay and the recovery percentage of each method was calculated and evaluated by standard curve. All analyzes were performed in duplicate. Along with reviewing the methods, a sample without viral inoculation (negative

control sample) and a direct vaccine sample (positive control sample) were tested for quality control.

Results: In four compared methods, the method that using, TGBE 3% and PEG 10%, has the highest efficiency (22.4%) for detecting enveloped viruses from the surface of lettuce leaves. However, other methods with lower IBV recovery rates are able to detect these group of viruses.

Conclusion: Our results show that higher concentration of TGBE could better wash the virus from the surface of lettuce leaves, while lower concentration of PEG has better results and this method is an optimal method with a good recovery rate for the detection of enveloped viruses.

Keywords: vegetable, method, enveloped virus

Comparison of blood glucose and anthropometric indices with different levels of physical activity in male employees (Research Paper)

Mohammad hosein aghidemand ,[1,*] vahab khanahmadi,[2]

1. Allameh Tabataba'i University
2.

Introduction: Background & Aims of the study: Physical activity and lifestyle is one of the important and influential factors on human health. Also, anthropometric and blood glucose indices are directly related to the level of health of individuals. Therefore, the aim of the present study was to compare blood glucose and anthropometric indices with different levels of physical activity in office workers.

Methods: A total of 154 available male employees participated in this study. First, demographic information was collected and recorded. The International Physical Activity Questionnaire (IPAQ) was used to determine their level of physical activity. Based on the results of the physical activity level questionnaire, the subjects were classified into four levels of physical activity (low, medium, balanced, high). Then, blood glucose samples were taken from all subjects for 12 hours. Then anthropometric indices of the body including body mass index (BMI), waist circumference (WC) and waist to hip ratio (WHR) were measured and recorded. Also, ANOVA statistical test was used for intergroup comparison. All statistical analyzes were performed using SPSS software version 21.

Results: The results of the present study showed that there was a significant difference between individuals with low and high levels of physical activity for BMI and WHR indices ($p < 0.05$). On the other hand, no significant difference was observed between subjects with different levels of physical activity for fasting blood glucose and WC levels ($p = 0.1$, $p = 0.5$).

Conclusion: The higher the level of physical activity of office workers, the better the levels of anthropometric indicators and increase health among office workers.

Keywords: Physical activity, BMI, office staff, fasting blood glucose

Comparison of Deep Brain Stimulation Targets in Parkinson's disease: A systematic Review (Review)

Hushyar Azari,[1,*]

1. Urmia University of Medical Sciences

Introduction: Deep brain stimulation (DBS) is regarded as an important therapeutic choice for Parkinson's disease (PD). The two most common targets for DBS are the subthalamic nucleus (STN) and globus pallidus (GPi). This review was conducted to compare the clinical effectiveness of these two targets.

Methods: A systematic literature search in electronic databases: Embase, Cochrane Library and PubMed were restricted to English language publications 2010 to 2021. Specified MeSH terms were searched in all databases. Studies which evaluated the Unified Parkinson's Disease Rating Scale (UPDRS) III were selected by meeting the following criteria: (1) compared both GPi and STN DBS; (2) had at least three months follow-up period; (3)at least five participants in each group; (4)conducted after 2010. Study quality assessment was performed using the Modified Jadad Scale.

Results: 3577 potentially relevant articles were identified, of these, 3569 were excluded based on title and abstract, duplicate and unsuitable article removal. Eight articles satisfied the inclusion criteria and were scrutinized (458 PD patients). According to Modified Jadad Scale, the majority of included studies had low evidence quality which was a limitation of this review. 5 studies reported no statistically significant between-group difference for improvements in UPDRS ш scores. At the same time, there were some results in terms of pain, action tremor, rigidity, and urinary symptoms, which indicated that STN DBS might be a better choice. Regarding the adverse effects, GPi was superior.

Conclusion: It is clear that other larger randomized clinical trials with longer follow-up periods and control groups are needed to decide which target is more efficient for deep brain stimulation in Parkinson’s disease and imposes fewer adverse effects on the patients. Meanwhile, STN seems more reasonable according to the results of this systematic review.

Keywords: brain stimulation, globus pallidus, Parkinson’s disease, subthalamic nucleus

Comparison of HDL-C and LDL-C in men and women with high plasma cholesterol level: A year population-based study in Tehran 2019-2020 (Research Paper)

Gevik karpians ,[1,*]

1. medical group

Introduction: Hypercholesterolemia is one of the modifiable risk factors for atherosclerosis and cardiovascular diseases. The relation of cholesterol in creating coronary heart disease (CAD) has been specified. According to statistics announced by the Ministry of Health and Medical Education, 150,000 deaths due to stroke are recorded annually in Iran, Prevention and treatment of hypercholesterolemia and other lipid abnormalities require reliable data regarding the current prevalence of these abnormalities in the country. This study aims to determine the current prevalence of lipid abnormalities in Tehran.

Methods: In this article, comparisons of HDL-C and LDL-C in men and women between the ages of 45 to 65 years with equal or more than 200 mg/dL cholesterol level have been done. Data were collected according to a standard protocol. It was found that 167 women and 130 men had equal cholesterol and more than 200 mg/dL. After determining the final number of people in each group for statistical analysis using the amount of cholesterol, other parameters evaluated by HDL-C and LDL-C were also collected and statistical analysis was performed, for this purpose comparison of these factors was performed using chi square, t-test, and bar chart in both male and female populations.

Results: Results shows the means of cholesterol level were 230.5 mg/dL in men and 216.5 mg/dL in women, the cholesterol level is more desirable in women compared to men, even in cases above the normal range. The LDL-C study found that the mean LDL-C in men was 140.47mg/dL in the border high range (130-159 mg/dL), but the mean in the female population equal to 122.7 mg/dL is in the above optimal range (100-129 mg/dL). Only 3.07% of men and 25.15% of women had optimal LDL-C level. Also, in investigating HDL-C, women have a more desirable position compared to men. The means of HDL-C level were 40.2 mg/dL in men and 45.2 mg/dL in women. Pearson's correlation was used to analyze the association between all studied parameters. The values $P < 0.05$ were considered statistically significant.

Conclusion: The cholesterol level is more desirable in women compared to men, even in cases above the normal range. The comparison of HDL-C and LDL-C in men and women with high cholesterol level has been completed.

High LDL-C is the main lipid abnormality in this population. The majority of men in this study did not meet the desired level of LDL-C and HDL-C. Public health preventive policies should be made and implemented to better manage dyslipidemia.

Keywords: atherosclerosis, cardiovascular disease, cholesterol, high density lipoprotein cholesterol, low dens

Comparison of Sensitivity and Specificity of Pap smear and Polymerase Chain Reaction Methods for Detection of Human papillomavirus; A Review of Literature (Review)

maryam malekian,[1,*] Muhammad Irani Estyar,[2]

1. bachelor of midwifery, Tehran University of Medical Sciences, Iran, Tehran
2. bachelor of nursing, Tehran University of Medical Sciences, Iran, Tehran

Introduction: Human papillomavirus (HPV) is one of the most common sexually transmitted infection which may lead to cervical cancer as the main cause of it. 4.5% of all cancers worldwide are attributable to HPV. With early diagnosis and treatment in health care services, cervical cancer and its complications are considered to be preventable. This study was aimed to compare the efficiency, sensitivity, and specificity of Pap smear and polymerase chain reaction (PCR) in detecting HPV.

Methods: A literature search was performed in Google Scholar, PubMed and SID databases using the keywords "human papillomavirus", "pap smear" and ""polymerase change reaction " to identify studies comparing Pap smear and PCR methods for the detection. No restrictions were considered.10 studies were included in this review.

Results: All samples that were positive by pop smear were also positive by PCR, however, there were positive samples detected by PCR which was negative by pop smear and in all studies, many positives samples were missed by pop smear technique. Although The Pap smear had high specificity, PCR-based HPV detection was more sensitive method and had the highest sensitivity.

Conclusion: in order to promote the quality of detection and high achievement of the maximum results, PCR diagnostic methods in addition to the Pap smear are needed and Pap smear method should be combined with PCR techniques according to the high error rate of Pap smear in detection.

Keywords: human papillomavirus, cervical cancer, Pap smear, Polymerase Chain Reaction

Comparison of the effects of extended release tolterodine and solifenacin in treatment of overactive bladder symptoms (Research Paper)

maryam hajihashemy,[1] Tahere Eftekhar,[2] Maryam Deldar,[3] Mamak Shariat,[4] Zinat Ghanbari,[5,*]

1.
2. Department of Obstetrics & Gynecology, Vali-e-Asr Hospital, Tehran University of Medical Sciences, Tehran, Iran
3. Department of Obstetrics & Gynecology, Vali-e-Asr Hospital, Tehran University of Medical Sciences, Tehran, Iran
4. Maternal, Fetal and Neonatal Research Center, Tehran University of Medical Sciences, Tehran, Iran
5. Department of Obstetrics & Gynecology, Vali-e-Asr Hospital, Tehran University of Medical Sciences, Tehran, Iran

Introduction: Overactive bladder (OAB) is defined as frequent and sudden urge to urinate that is difficult to control. Here we aimed to compare the effects of extended release tolterodine and solifenacin in treatment of OAB in Iranian population.

Methods: This was a prospective randomized clinical trial that was performed in 2021 in Imam Khomeini Hospital in Tehran on women with OAB. We collected demographic data of patients including age and history of patients. The 3-day frequency volume chart (FVC) and ICIQ-OAB questionnaire was then completed for each patient. The patients were randomly divided into two groups of A and B. An automated clinical trial service was used to assign patient number and provide the medication number indicated by the central randomization system. Group A received 4 mg of slow-release tolterodine and Group B received 5 mg solifenacin for 8 weeks. One month and two months after start of treatment, ICIQ-OAB questionnaire and the 3-day frequency volume chart (FVC) were obtained again.

Results: Totally, 51 patients in solifenacin group and 48 in tolterodine group completed the study. There was no significant difference between mean scores of ICIQ.OAB before treatment and one month after initiation of treatment between two groups (P> 0.05) but two months after treatment, the tolterodine group was significantly more than solifenacin group regarding mean scores of ICIQ.OAB (P <0.05). The mean score of ICIQ.OAB in both groups decreased over time (P <0.001). Two months after treatment, urgency in solifenacin group was significantly less than the tolterodine group (P <0.05). The average number of frequency, nocturia, urgency and the number of urinary leakage in both groups were significantly different in three times (P

<0.05). The mean of all 4 variables in both groups decreased significantly over time (P <0.05).

Conclusion: solifenacin was superior to tolterodine in diminishing of ICIQ score. According to FVC, solifenacin was better to diminish urgency and more patient in solifenacin group and became dry after two months.

Keywords: overactive bladder, solifenacin, tolterodine

Comparison the different immunogenicity methods of experimental Neospora caninum vaccine in mice (Research Paper)

zahra zarenejad,[1] Mohammad mehdi Namavari,[2,*] Ahad olyaei,[3] Fatemeh Dabiri,[4]

1. Department of Veterinary Medicine, Kazerun Branch, Azad University, Iran
2. Shiraz Branch, Razi Vaccine and Serum Research Institute, Agricultural Research, Education and Extension Organization (AREEO), Shiraz, Iran
3. Department of Veterinary Medicine, Kazerun Branch, Azad University, Iran
4. Shiraz Branch, Razi Vaccine and Serum Research Institute, Agricultural Research, Education and Extension Organization (AREEO), Shiraz, Iran

Introduction: Neospora caninum is a pathogenic coccidial intracellular protozoan of the sarcocyste family that is very common in dairy and beef cattle and can lead to abortion or birth of an infected calf. Neospora caninum is a major economic challenge in the field of husbandry animal around worldwide and can cause abortion, stillbirth, calf mortality, poor calf production, re-breeding and reduced milk production. One of the most effective ways to control infection is to use vaccination. Neospora caninum live-attenuated strain with adjuvant is able to create good immunity in animals. In this study, we evaluated and compared the best immunogenicity method with experimental vaccine of Neospora caninum with adjuvant in BALB / C mice as the best laboratory model for neosporosis.

Methods: Thirty mice were randomly divided into six equal groups, including the control groups, live-attenuated strain with aluminum hydroxide adjuvant, live-attenuated strain with combined adjuvant separately groups by intramuscular injection, subcutaneous injection, intraperitoneal injection and orally; all were immunized in two phases with four weeks apart. Agglutination and ELISA tests were used to assess the humoral immune response and gamma interferon test was used to measure cellular immunity.

Results: The results showed that the immunized group with live-attenuated strain with combined adjuvant by subcutaneous injection had the highest humoral immune response and the immunized group with live-attenuated strain with combined adjuvant by intraperitoneal injection and also by intramuscular injection had the highest cellular immune response.

Conclusion: Overall, the results of this study showed that the selection of an appropriate method for vaccination is effective on humoral and cellular immunity. The live-attenuated vaccine of Neospora caninum with combined adjuvant in mice in different ways is induce an effective humoral and cellular immune response and immunizing mice with this method is safe and

completely effective. Therefore, it is suggested that this experimental vaccine and intramuscular or subcutaneous injection method be used in additional research in order to obtain a functional vaccine used to control the infection caused by Neospora caninum in farm animals such as cattle and sheep.

Keywords: Neospora caninum, immunization, mice

Computational Design of Cyclic Peptide Inhibitors with potential to block SARS-CoV-2 spike and human ACE2 protein-protein interaction (Research Paper)

Mohammadrezaforouharmanesh,[1,*]

1.

Introduction: Introduction COVID-19 global pandemic is caused by a coronavirus named Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The spike structural protein of SARS-CoV-2 mediate the host attachment and viral entering to host-cells by protein-protein interactions (PPIs) with the angiotensin-converting enzyme 2 (ACE2) as a host cellular receptor. Design peptide to block these critical PPIs is a new strategy to combat COVID-19 pandemic. Formation of disulfide bridges to cyclized peptide is preferable method in order to improve its activity and bioavailability as well as to prevent its digestion by protease enzymes. The aim of this study is to design cyclic peptide inhibitors to block SARS-CoV-2 spike and human ACE2 interaction by using computational PPIs analysis, molecular docking and drug scan methods

Methods: The computational peptide design is based on the key residues leading the SARS-CoV-2 spike and human ACE2 interactions. First, the crystal structure of SARS-CoV-2 spike receptor-binding domain bound with ACE2 with 6M0J PDB ID was obtained from RCSB PDB (https://rcsb.org). DIMPLOT program from LigPlot+ software (https://www.ebi.ac.uk/thornton-srv/software/LigPlus/) was used to analysis PPIs leading residues. 2D maps generated by DIMPLOT showed hydrogen bonds and hydrophobic contacts in PPIs and used for creating a list of residues in PPIs site for inhibitory peptide design. Then, 4 peptides were design and PEP-FOLD web-server (https://bioserv.rpbs.univ-paris-diderot.fr/services/PEP-FOLD3/) was used for de novo prediction of peptide 3D structures. PEP-Cyclizer (https://bioserv.rpbs.univ-paris-diderot.fr/services/PEP-Cyclizer/) was utilized for design of head-to-tail peptide cyclization. Molecular dockings of designed cyclic peptides with SARS-CoV-2 spike were conducted using Haddock web-server (https://wenmr.science.uu.nl/). ToxTree (http://toxtree.sourceforge.net/) and FAF-drugs4 (https://fafdrugs4.rpbs.univ-paris-diderot.fr/) were used for drug scan and ADME-Tox prediction assay. The physicochemical descriptors and properties of cyclic peptides were computed by these tools

Results: PPIs anaylis were done by studying critical residues leading SARS-CoV-2 spike and human ACE2 interactions. These residues were used for computational peptide design. Four cyclic peptides including CEADLFYQSSLASC, CIEEQAKTFLDKC, CIEEQAKTFLDKFNHEAEDLC, and CFNHEAEADLFYQSSLASC were designed. The molecular docking

results showed that among the designed cyclic peptides CIEEQAKTFLDKC with highest binding energy to SARS-CoV-2 spike protein and the most acceptable properties derived from drug scan studies have great potential to inhibit interaction of spike and ACE2 receptor and blocking viral entry to host cells. No mutagenic and carcinogenic effects were predicted for these peptides. Also, good bioavailability was predicted for them

Conclusion: Our computational results including residues analysis in PPIs site, molecular docking, and drug scan studies revealed the cyclic peptides with the potential to act as SARS-CoV-2 spike protein inhibitor to block coronavirus entry to human cell. These peptides are the candidate to select as SARS-CoV-2 entry inhibitor to design and development of new drugs to treatment of COVID-19 pandemic. Note that this computational study need more wet lab and dry lab analysis

Keywords: COVID-19, SARS-CoV-2, Protein-protein interactions, Spike, ACE2

Considering the effect of fermented soybean meal by bacillus subtilis on CD177 gene expression in septic rat (Research Paper)

Fahimeh Ganjifar,[1] Azadeh Rasooli,[2,*] Reza Hojihosseini,[3]

1. Department of Biochemistry, Faculty of Science, Payame Noor University, Tehran, Iran
2. Department of Biochemistry, Faculty of Science, Payame Noor University, Tehran, Iran
3. Department of Biochemistry, Faculty of Science, Payame Noor University, Tehran, Iran

Introduction: Introduction Sepsis as life-threatening acute organ dysfunction secondary to infection affects more people each year. After sepsis, the immune response is associated with a major inflammatory response. Neutrophils have various functions in the immune system in sepsis. CD177 as an important neutrophil gene encodes the glycoprotein of the membrane that the expression of this gene is increased during bacterial infections. So, the measurement of CD177 mRNA levels could be a useful diagnostic tool for distinguishing some diseases such as sepsis. Due to the high incidence of sepsis and high risk of death globally, this syndrome needs urgent treatment. Natural resources like soybean meal as an important source of protein are the richest bio-resource of drugs. Also, fermented soybean meal by mixed microorganism shows probiotic properties that can be as an alternative for antibiotics. Therefore, in this study, the anti-inflammatory effect of fermented soybean meal extract by bacillus subtilis on septic rat was investigated.

Methods: Methods Sixty male Wistar rats (250±20 g) were purchased from the Pasteur Institute of Iran. Rats randomly divided into 6 groups (n=10) including Control groups (without any surgery and treatment), laparotomy groups (LAP) (Shock surgery groups without ligation and puncture of cecum), CLP groups (cecal ligation and puncture without treatment), and treatment groups (5%, 10% and 20% of fermented soybean meal after sepsis induction). The soybean meal was fermented with bacillus subtilis, and then its extract was prepared for further analysis (All procedures was done according Miri et al., (2021) article). After 48 h, the rats were euthanized and tissues were collected for Real time PCR analysis. Real-time PCR reactions were performed using SYBR Green PCR Master Mix (QIAGEN, Germany) with Rotor-Gene Q system (QIAGEN, Germany).

Results: Results The results of this study revealed that the expression of CD177 gene as inflammatory factor increased by LAP and CLP surgery compared with control group in both lung and spleen tissues and animal treatments with fermented soybean in all doses have been effective in decreasing the expression level of the CD177 gene compared with the CLP

group ($P < 0.05$). It is noteworthy that fermented soybean meal at a dose of 5% was better in diminishing of CD177 gene expression in both tissues as compared with the dose of 10 and 20 %.

Conclusion: Conclusion Finally, the results showed that treating rats with fermented soybean meal immediately after sepsis induction reduced sepsis-induced lung and spleen tissues damage. Therefore, it can be concluded that anti-inflammatory effects of fermented soybean meal could be a potential therapeutic agent for tissues injury in sepsis induced by CLP.

Keywords: Keywords Bioactive peptides, Bacillus subtilis, CD177, Sepsis, Anti-inflammatory effect

Construction an Efficient Strain for Purity of TEV-Labeled Recombinant Proteins (Research Paper)

Naieme Goharifar,[1,*] Mahbube Foruzamfar,[2] Kianoosh Dormiani,[3]

1. Royan institute
2. Royan institute
3. Royan institute

Introduction: Peptide tags are protein sequences that are used in recombinant proteins mainly in order to increase the solubility or facilitate the purification of the proteins. Generally, the used tags need to be removed accurately and appropriately after the production and purification of the recombinant proteins. Using the some proteases such as TEV protease is a common method to remove the fusion tags. This protease is a highly sequence-specific cysteine protease, produced by Tobacco etch virus (TEV) and considered as one of the best endpeptidases for removing of the tags. We hypothesized that by induction of the bacterial cells to produce this protease at an appropriate time after production of the target recombinant protein, it is possible to digest and separate the tag from the target protein when the function of dissolution tag to improve recombinant protein solubility is completed. Accordingly, in the present study, a plasmid was constructed that exclusively encoded TEV protease using arabinose as the inducer. This vector was independent of the vector used to express the recombinant protein. In this plasmid, TEV encoding sequence was located under the BAD promoter, and p15A Ori, which is compatible with pBR322 Ori in pET expression vectors was used. We also used Neo-Kan resistance gene in the plasmid that allows the selection of transformed bacteria that already had pET vector with Amp resistance gene. This approach ensures that TEV encoding vector and pET vector expressing the recombinant protein to be compatible and can remain in the bacterial cells simultaneously. Following transformation of constructed TEV plasmid to E. coli, a new subspecies is acquired in which TEV protease is expressed by induction with arabinose that results in controlled production of TEV protease at an appropriate time to ensure that removal of the tag is taken place after completion of folding of recombinant protein.

Methods: First, the specific primers that contained suitable restriction enzymes at the 5' ends were designed for amplification of GST tagged TEV coding fragment (GST.TEV) form pGEX-4T1 vector. Amplified GST.TEV was cloned into a T vector and subsequently sub-cloned into the expression vector pBAD-GIIIA, called pBAD/GST.TEV. The transcription terminator (TT) sequence was then amplified from pBAD-GIIIA vector by proper primers and sub-cloned downstream of GST.TEV fragment in the pBAD/GST.TEV. The resulted vector was named pBAD/GST.TEV/TT. Moreover, the coding

sequence of neomycin-kanamycin phosphotransferase (Neo-Kan) was amplified from pEGFPC1 vector by the suitable primers and was sub-cloned in pBAD/GST.TEV/TT, downstream of transcription terminator that resulted pBAD/GST.TEV/TT/Neo-Kan. At the end, the p15A Ori segment was amplified from the pG.TF2 vector by designed primers and sub-cloned into pBAD/GST.TEV/TT/Neo-Kan downstream of Neo-Kan fragment. The constructed final vector was pBAD/GST.TEV/TT/Neo-Kan/p15AOri, which was briefly called pBAD/GST. Also, the accuracy of all cloned sequences was confirmed by DNA sequencing. Finally pBAD/GST plasmid was used to transform Shuffle T7 Express E. coli cells and the expression of soluble TEV protease was confirmed using SDS-PAGE. The activity of the recombinant TEV protease was evaluated in the Shuffle cells that were previously transformed by a pET32 vector expressing IGF-1 tagged with Thioredoxin (TRX).

Results: In this study, a new subspecies of Shuffle T7 Express E. coli was obtained by transformation of an expression plasmid, which could produce the soluble and active TEV protease

Conclusion: This protease could cleave its specific site between TRX and IGF-1 in the host bacterial cells and separate TRX tag from the recombinant IGF-1, which was expressed by an independent pET vector. Therefore, by this approach there is no need to digest the recombinant fusion protein after extraction from the bacteria. Indeed, in vivo digestion of recombinant fusion protein can have a significant effect on facilitating and reducing the costs of downstream purification process.

Keywords: TEV protease, Protein tag, Recombinant protein, Fusion protein, Shuffle T7 Express E. coli

Coronaceous period and Covid-19 pandemic; the possible consequences of destroying natural environments and biodiversity (Review)

Zahra Sheykhrezaee,[1] Saba Tabarsi,[2] Kimiya Nazari,[3] Salar Karjalian,[4] Fatemeh Haji-Mohammad-Hassan,[5] Alireza Golnaraghi,[6,*]

1. Department of Nature & Health, BoomZista Institute,, British Columbia,
2. Department Plant Protection, Science and Research Branch, Islamic Azad University
3. Department Plant Protection, Science and Research Branch, Islamic Azad University
4. Department Plant Protection, Science and Research Branch, Islamic Azad University
5. Department Plant Protection, Science and Research Branch, Islamic Azad University
6. Department of Biodiversity, BoomZista Institute,

Introduction: Scientists have been working for years to find a link between the loss or change in biodiversity and the emergence and spread of emerging diseases. Although ecologists have been warning of such a connection for decades, little attention had been paid to this challenging issue before Covid-19 pandemic and its subsequent serious problems. We named this time period as “Coronaceous period’ due to the profound and comprehensive effects of the Covid-19 pandemic on human life. This period and the serious issues have made researchers think deeply about the main causes and roots of recent outbreaks and find a solution to deal with them. Analysis of multiple biological communities in six different continents of the globe provide growing evidence of a high association between biodiversity loss and disease prevalence. Studies have shown that over the past few decades, the prevalence of diseases such as acute respiratory syndrome (SARS) and avian influenza, which are transmitted from animals to humans, has increased. This phenomenon is probably a direct result of the increasing connection between humans, wildlife and livestock, as people migrate and live in underdeveloped areas. Obviously, human interactions with animals occur more on the border of the expansion of human habitation to the pristine natural environment. One of the key questions is whether declining biodiversity, which is inevitably associated with human expansion across rural and natural boundaries, increases the range of pathogens that can be transmitted from animals to humans. Research results show that the answer in many cases is “yes”, because biodiversity loss, due to deforestation and change of land use, usually leads to the replacement of a few species instead of the majority of species in the natural environment, and these substituted species can host pathogens that transmit to humans. Studies have revealed that in this situation, the population of some mammals such as bats, rodents,

and various primates increases; this pattern is consistent with the pattern of Ebola outbreaks in Africa. Among wildlife, bats have easily adapted to human environments, such as homes, barns, farms, and gardens, where they have found suitable ecosystems to thrive. Bats play a key role in the evolution of coronavirusesare and are the main hosts of alphacoronaviruses (αCoV) and betacoronaviruses (βCoV). Their path of evolution in bats has resulted in the resistance of the hosts to viral pathogens; however, these viruses can easily attack other species, including humans. During the long time of evolution, many recombination and modifications, including one important modification to use ACE2 as a receptor in host cells, have occurred in these viruses that increased their potential for interspecies transmission. According to new researches, many factors have been involved in the occurrence of the Covid-19 pandemic: deforestation, changes in forest habitats, poorly regulated agricultural surfaces and mismanaged urban growth, as well as wildlife trade, growing and consumption, to mention but a few. On the other hand, we need a healthy immune system to overcome infectious diseases such as Covid-19; having such an immune system is impossible without the support of diverse microbiomes. The destruction that is being done by humans, e.g., unregulated urbanization, also largely affect microbial biodiversity; some of them, called our “old friends microbes” and found in natural environments around us, are crucial for training, regulating or bolstering our immune system. Having a weak immune system is one of the main reasons for the more mortality rates and disease severity in patients infected by the coronavirus. Some researchers believe that the rapid increase in non-infectious health issues, such as asthma and inflammatory bowel diseases, in urban areas also links with the loss of microbial biodiversity and less exposure to them.

Methods: This_is_a_review_article.

Results: This_is_a_review_article.

Conclusion: Studies reveal an increase in diseases outbreaks in recent decade, including Covid-19 pandemic, which seems to be related with the destruction of natural environments and biodiversity by humans. Obviously, efforts to preserve nature will only be effective if they can address the cultural and economic roots of such behavior and eliminate them. Scientists and policymakers also need to be more inclusive of rural boundaries with natural environments, while addressing issues of public health, the environment and “sustainable development”. However, it is very clear that if we, humans, continue our destructive behavior, we should expect more outbreaks in the future.

Keywords: pandemic, Covid-19, biodiversity loss, land-use change, nature destruction

Correlation between renin-angiotensin-aldosterone system in patients with cancer and COVID-19 infection (Review)

Javad Yaghmoorian Khojini,[1] Ali Osmay Gure,[2] Kamran Ghaedi,[3,*]

1. Department of Medical Biotechnology, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
2. Department of Medical Biology, Acibadem University, Istanbul, Turkey
3. Department of Cell and Molecular Biology and Microbiology, Faculty of Biological Science and Technology, University of Isfahan, Isfahan, Iran

Introduction: Coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus. It emerged as pneumonia cases in Wuhan, China for the first time and rapidly spread across the world. The entry receptor of SARS-CoV2 known as ACE2 constitutes the Renin Angiotensin System (RAS) which performs different functions in different cases such as cancer, vascular homeostasis and many other body processes. It is expressed in many organs such as liver and brain too. The aim of this study was to investigate the relationship between RAS and COVID-19.

Methods: This systematic review study was done using various update articles, books and authoritative scientific sites.

Results: Coronavirus disease 2019 (COVID-19), a rapidly evolving pandemic infecting more than 150 million people worldwide with more than 4 million deaths according to the World Health Organization (WHO) to date. One of the concerns for patients suffering with the cancer with COVID-19 is the function of the renin angiotensin aldosterone (RAS) system. This system is a hormonal system that regulates blood pressure and body fluid balance and plays an important role in cancer regeneration of the tumor microenvironment, as well as tumor growth and metastasis of cancer cells throughout the body. However, COVID-19 disease modifies the normal function of this system using the angiotensin-converting enzyme (ACE2) receptor. This condition disrupts the function of the intravascular layer in many tissues and organs of the body. The RAS is composed of two pathways and both pathways begin with renin and these include the ACE-mediated vaso-constrictive side and the ACE2-mediated vaso-dilative side. ACE2 is the entry receptor for SARS-CoV-2. Once COVID-19 infection has taken place, virus binding is likely to prevent ACE2 mediating its usual pneumoprotective effects. The virus transmembrane spike glycoprotein (S protein) is essential for binding to the cellular membrane ACE2 and for the attachment of the virus to the target cells. ACE2 is localized in lung alveolar epithelial cells, small intestine, enterocytes arterial endothelial cells and other parts of the body. Therefore the lungs, and small intestine are the likely sites of SARS-CoV-2. The expression of ACE2 in the lining of blood vessels it could contribute to the risk of thrombotic events in patients with

COVID-19. Another discovery is that the ACE2 gene is carried on the X chromosome which may possibly account for the apparent increased susceptibility of men to COVID-19. Further studies on this topic are undergone.

Conclusion: Because some types of cancer can be treated with ACE, the process of further disruption of the RAS system caused by COVID-19 can lead to much more serious complications in this type of cancer treatment process. So because of the interaction between ACE2 and the coronavirus virion could act as a target for vaccines. RAS inhibitor drugs targeting the ACE side of the system, and hence increasing activity of the ACE2 pathway, have the potential to reduce COVID-19. It is hoped that by conducting more studies, researchers around the world will be able to gain more knowledge about the processes and factors that contribute to the increased pathogenicity of COVID-19.

Keywords: COVID-19, ACE2, RAS, pathogenicity, treatment

Correlation of chronological age, dental age and skeletal maturation in 7 to 17 years old population in south Iran (Research Paper)

Sina Behzadipour,[1,*] Narges Arya,[2] Shekufeh Mohammadpour,[3] Sadaf Rezai,[4] Mohammad Mehdi Khaleghi,[5] Mitra Evazzadeh,[6]

1. Student Research Committee, Busheher University of Medical Sciences, Bushehr, Iran
2. Student Research Committee, Busheher University of Medical Sciences, Bushehr, Iran
3. Student Research Committee, Busheher University of Medical Sciences, Bushehr, Iran
4. Student Research Committee, Busheher University of Medical Sciences, Bushehr, Iran
5. Student Research Committee, Busheher University of Medical Sciences, Bushehr, Iran
6. Student Research Committee, Busheher University of Medical Sciences, Bushehr, Iran

Introduction: Age estimation is an important part of forensic Odontology and orthodontic treatment planning. Environment have been proved to have an effect on growth. Since Willems's dental age estimation has not been studied in southern Iranian population, the aim of the present study was to assess the correlation of chronological, dental and skeletal age in Bushehr in 2020.

Methods: In the present cross-sectional study, 85 pair of orthopantograms and cephalograms of 8-17 years old children and adolescents were selected. Dental age was determined using Willems's method and skeletal maturation was determined using the cervical vertebrae method. Tooth malformation, pathologic conditions involving roots, present orthodontic treatment and images with low quality were excluded. Two dental interns, a radiologist and an orthodontist did the interpretations separately. Dental age and skeletal maturations were compared among students and specialists.

Results: Of 85 samples, 34 were for boys and 51 were for girls. The mean chronological, and dental age was 12.82±2.38 and 13.16±2.83 respectively. The mean difference was 0.34±1.30. Dental and chronological age had a strong correlation (0.880) in the present study. The correlation between students and specialists in determining skeletal age was overall moderately and strong (0.60-0.80). The correlation between students and specialists in determining dental age was overall very strong (more than 0.90).

Conclusion: The Willems' method was applied in determining the age of the samples in the present study. The correlation between students and

specialists in determining dental age was overall very strong, showing that dental age estimation using calcification stages is easier than the cervical vertebrae maturation method.

Keywords: Dental age, Calcification, Skeletal maturation, Willems, Radiography

COVID-19; a global challenge for improving mental health (Review)

Nafiseh Soudi,[1,*] Shiva Pouyanfar,[2]

1. Department of Laboratory Science-Tabriz Faculty of Paramedicine -Tabriz University of Medical Science
2. Student Research Committee, Alborz University of Medical Sciences, Karaj, Iran

Introduction: The sudden onset of the Coronavirus as a global pandemic has further threatened people's lives and mental health. Given the uncertainty and unpredictability of its initial outbreak and the lack of sufficient knowledge about the effects and characteristics of this newly emerging virus, we require specific strategies to control and reduce the adverse outcomes of this disease. Quarantine, social distancing, and forced lifestyle changes are some essential strategies offered to control this disease, which given the social nature of humans, can affect different aspects of people's mental health.

Methods: By reviewing some of the researches in this field, the required information was extracted and examined.

Results: Depression, anxiety, and stress are some of the outcomes that appear more often than before following the outbreak of this disease. The role of stress and anxiety control to prevent this disease and during recovery as a crucial factor in the patient's recovery process has become very important. Dealing with different psychological changes after recovering from this disease in individuals and after the end of the pandemic in the global population will be immensely challenging.

Conclusion: Therefore, from the therapeutic and preventive point of view and regarding the strengthening people's cognitive flexibility to face and deal with other similar diseases in possible future crises, paying attention to individuals' mental health and trying to improve it become more important than ever.

Keywords: Covid-19; Mental health.

covid19 and bradykinin storm (Review)

AmirHosein Yari,[1,*] Anahita Samadzadeh,[2] Zahra Ebadi,[3]

1. Department of Biology, Faculty of Microbiology, Tabriz Branch, Islamic Azad University, Tabriz, Iran
2. Department of biology, Faculty of Basic Sciences, University of Maragheh, Maragheh, Iran.
3. Department of biology, Faculty of Basic Sciences, Azarbaijan Shahid Madani University, Tabriz, Iran

Introduction: Since December 2019, the Novel Coronavirus, commonly known as COVID-19, has been spreading across the globe. It poses a major danger to the community healthcare systems of every country on Earth. Despite the fact that the influenza pandemic began in 1918, Coronavirus illness 2019 has emerged as the most serious public health epidemic to have occurred since that time. The need of learning more about COVID-19's characteristics and interactions with human host cells cannot be overstated in order to develop effective COVID-19 treatments. Despite the fact that the severity of COVD-19 illness varies from patient to patient, the vast majority of them suffer from typical cold symptoms that develop to moderate Pneumonia. The presence of spike glycoproteins on the virus's envelope gives it a crown-like appearance under an electron microscope (corona is the Latin word for crown). Patients with moderate illness recover within a week, whereas those with severe disease have significant respiratory difficulties as a result of alveolar destruction, which ultimately results in mortality, particularly in the elderly with pre-existing diseases. Patients with moderate illness recover within a week, whereas those with severe disease have significant respiratory difficulties as a result of alveolar destruction, which ultimately results in mortality, particularly in the elderly with pre-existing diseases. Numerous polypeptides have been shown to have an effect on the smooth muscle of blood arteries. Oxytocin, vasopressin, angiotensin, anaphylatoxin, leucotaxine, and bradykinin are a few examples (plasma kinin) Brady kinin is one of the most obscure of these compounds. Bradykinin is formed when factor XII, prekallikrein, and high-molecular-weight kininogen interact with negatively charged inorganic surfaces (silicates, urate, and pyrophosphate) or macromolecular organic surfaces (heparin, other mucopolysaccharides, and sulfatides) or when they clump together on the surface of cells. Bradykinin binds to endothelial B1 and B2 receptors and exerts a variety of pharmacological and physiological effects, including reduced blood pressure, increased vascular permeability, and stimulation of typical inflammatory symptoms such as vasodilation, heat, oedema, and pain. The virus enters the body via the protein ACE2, which is a component of the RAS hypotensive axis that works to prevent hypertension. It is a powerful component of the vasopressor system that causes hypotension and vasodilation.

Methods: Bradykinin is destroyed by ACE and increased by the angiotensin1-9 generated by ACE2. Earlier research has shown that bradykinin produces pain and causes blood vessels to dilate and leak, As a consequence, the surrounding tissue becomes swollen and inflamed. The analysis revealed a rise in the synthesis of a chemical called hyaluronic acid and a significant reduction in the enzymes capable of degrading it. Hyaluronic acid is capable of absorbing 1,000 times its own weight in water and forming a hydrogel. Bradykinin-Storm-induced fluid leaking into the lungs, coupled with an excess of hyaluronic acid, would likely result in a Jello-like material that prevents oxygen absorption and carbon dioxide release in the lungs of seriously afflicted patients. Patients with COVID-19.

Results: Thus, Garvin et alresults .'s suggest that the Bradykinin Storm may be responsible for the more severe COVID-19 symptoms. Although considerable attention has been focused on the lungs because to the need for ventilator assistance in advanced illness, COVID-19 also affects the gut, liver, kidney, heart, brain, and eyes. Cardiovascular damage occurs in almost one-fifth of hospitalized patients. This may be caused directly by viral infection and is consistent with the high expression of the SARS-CoV-2 receptor ACE2 in cardiac tissue. COVID-19 has been implicated in neurological disease following an MRI examination of COVID-19-positive individuals with encephalopathy symptoms in France showed elevation in leptomeningeal spaces and bilateral frontotemporal hypoperfusion. which are associated with increased cerebral vascular permeability. Direct viral infection and kidney injury were also found, most notably in the proximal tubules.

Conclusion: These last two results are unsurprising in light of the increased expression of ACE2 in these tissues relative to other tissues. Recent study indicates that some traditional Chinese medicines (TCMs) have anti-inflammatory, anti-renin-angiotensin system (RAS)-mediated bradykinin storm (RBS), and antiviral properties. The snake-derived bradykinin-potentiating peptide (BPP-10c) significantly reduces angiotensin II levels by inhibiting ACE, increasing bradykinin-related effects on the bradykinin 2-receptor, and increasing nitric oxide-mediated effects, and thus may be the most effective option to consider when developing an anti-SARS-COV-2 drug.

Keywords: Corona virus, sarscov2, bradykinin

Creating an efficient strain for purity of TEV-labeled recombinant proteins (Research Paper)

Naieme Goharifar,[1,*]

1. Royan institute

Introduction: Peptide tags are protein sequences that are used in recombinant proteins mainly in order to increase the solubility or facilitate the purification of recombinant proteins. Generally, the used tags need to be removed accurately and appropriately after the production and purification of recombinant proteins. Using the proteases such as TEV proteases is one way to remove the tags. This protease is produced by Tobacco etch virus (TEV). Simultaneous production of this protease in the target recombinant protein-producing bacterium causes the isolation of solubilizing tags from target proteins. The aim of this study is the construction a TEV protease-producing expression vector and its transform to an appropriate species of E. coli, which is used to produce recombinant protein. In this way, a new subspecies is constructed in which the structure producing the TEV protease in a controlled manner produces appropriate amounts of TEV protease.

Methods: First, the specific primers that contained suitable restriction enzymes at 5'ends were designed for amplification of GST.TEV fragment form pGEX-4T1 vector.Then it was cloned into the T vector as cloning vector and subsequently cloned into the expression vector pBAD-GIIIA. After that, the terminator fragment was amplified from pBADgIIIA vector by proper primers and cloned downatream of GST.TEV fragment in the pBAD-GIIIA vector. The NEO.KNA fragment was amplified from EGFPC1 vector by proper primers and was cloned in pBAD-GIIIA downstream of terminator fragmentvector. At the end, the p15A Ori fragment was amplified from the pG.TF2 vector by appropraite primers and subcloned into the pBAD-GIIIA downstream of NEO.KAN fragment. All fragments was are verified by sequencing.

Results: In this study, a new subspecies of E. coli is obtained with construction of recombinant vector which could produces the soluble active TEV protease.

Conclusion: This protease could remove dissolution tags from recombinant proteins with suitable digestion sites. In this situation, the dissolution tag used upstream or downstream of the recombinant protein and removed in the host bacterial cells that can have a significant effect in facilitating and reducing the costs of downstream purification processes.

Keywords: TEV protease, Protein tag, Recombinant protein, Fusion protein, Expression vector, E. coli

CRISPR/Cas system and its applications in drug resistance Breast cancer (Review)

Hanieh Ataollahi,[1,*] Helia Ramezani,[2]

1. Faculty of Biological Science, Department of Biotechnology, Islamic Azad University, North Tehran Branch, Tehran, Iran.
2. Faculty of Biological Science, Department of Biotechnology, Islamic Azad University, North Tehran Branch, Tehran, Iran.

Introduction: Introduction: Many bacterial and archaea organisms use CRISPR/Cas systems (clustered regularly interspaced short palindromic repeats/CRISPR associated) to protect themselves from mobile genetic factors. These CRISPR/Cas systems are classified into six categories according to their composition and mechanism. Cancer is one of the main causes of death all around the world. It is caused by the accumulation of genetic and epigenetic modifications in 2 types of genes: tumor suppressor genes (TSG) and proto-oncogenes. In recent years, the development of CRISPR technology has revolutionized genomic engineering for cancer research ranging from basic science to translational medicine and primary cancer treatment. Breast cancer is one of the leading causes of cancer death in women worldwide, accounting for around 28% of new cancer cases. Clinical evidence indicates that drug resistance is a major barrier in the treatment of breast cancer. It makes the disease uncontrolled and leads to high mortality. Drug resistance causes breast cancer to spiral out of control and leads to high mortality, with more than 90% of treatment failures due to acquired and multidrug resistance (MDR). The development of new drugs with different targets is extremely time-consuming and expensive to avoid known resistance mechanisms. This review explains how CRISPR/Cas9 can be used to address problems associated with drug resistance in breast cancer by reversing resistance gene mutations, screening for resistance targets, and define drug therapy in breast cancer. In addition, we specifically discuss efficiency, modification of the protospacer adjacent motif (PAM), targeting selection, and application of CRISPR/Cas9.

Methods: Methods: The aim of this review study was to use new systems in the treatment of breast cancer and to provide solutions for drug resistance in the treatment process of this deadly cancer among women. 2010 to 2021 study was conducted. The search was performed by different keywords “CRISPR ", “CRISPR " and “CRISPR and Breast Cancer" and the articles were used based on the most appropriate titles and abstracts from various databases such as “PubMed”. “ScienceDirect”, “Springer”, “NCBI” and The results were obtained by studying the full text of the opted articles.

Results: Results: The emerging clinical trial has indicated that a gene-editing technique could be safe and effective in humans. US and Chinese teams intended to use CRISPR/Cas9 system in similar ways but on different types of cancers. The CRISPR/Cas9 system has been proposed as a therapeutic method to overcome drug resistance in chemotherapy-resistant cancers Blocking resistance factor(s) is an attractive strategy to further use existing anticancer agents. There are several strategies to enhance drug therapy, including altering membrane transport protein to increasing drug efflux, enhancing DNA repair and detoxification. In one study was tried to overcome doxorubicin-resistance cancer cells by using the CRISPR/Cas9 system to target MDR1. MCF-7/ADR cells were treated with doxorubicin after disruption of MDR1 by Cas9-sgRNA, and possible drug sensitivity recovery was examined. The potency of doxorubicin was enhanced in the cells treated with CRISPR/Cas9 expression construction using a proper delivery platform.

Conclusion: Conclusion: The use of specific targeting technologies will help us understand the mechanisms of signaling pathways such as the "genomic landscape" routes of breast cancer. Further insights into the molecular mediators of resistance will have a great impact on the ability to target genes or pathways that could overcome drug resistance for improving clinical outcomes. Therefore, although still exists technical limitations to the usage of the CRISPR/Cas9 system for targeting cancer genes in human patients, the prospects of gene therapy are nonetheless very exciting. CRISPR-based genome editing will serve as a critical tool.

Keywords: Keywords: CRISPR/Cas9, Breast cancer, Drug resistance

Cyanidin 3-O-Glucoside Induces the Apoptosis in the Osteosarcoma Cells through Upregulation of the PPARγ and P21: An In Vitro Study (Research Paper)

Hesam Adin Atashi,[1,*]

1. Young Researchers and Elite Club, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

Introduction: Osteosarcoma (OS) is known as the malignant tumors in the bone. Cyanidin 3-OGlucoside (C3G) has a potential to induce the apoptotic cell death in different cancer cells; however, the mechanisms of action for C3G have not been clarified yet. In this study, the apoptotic effects of C3G on three different osteosarcoma cell lines including Saso-2, MG-63, and G-292 (clone A141B1) were investigated.

Methods: The 24-hr IC50 of C3G for Saso-2, G-292, and MG-63 cells was evaluated by the MTT assay. Apoptosis induction in these cell lines after treatment with the C3G was approved by the Annexin V/PI flow cytometry. Changes at the mRNA expression level of PPARγ, P21, Bax, and Bcl-xl genes were investigated by real-time Polymerase Chain Reaction (PCR) technique, and P21 expression was further confirmed by the western blotting.

Results: The MTT assay results demonstrated that the 24-hr IC50 of C3G was equal to 110µg/ml for Saso-2 and G-292 cells while it was about 140µg/ml for the MG-63 cells. The results of real-time PCR clearly showed that treatment of the cells with 24hrs IC50 of C3G caused the upregulation of PPARγ, P21, and Bax genes. Moreover, western blot analysis confirmed that P21 protein overexpressed endogenously after treatment of the cells with the C3G, and it was more upregulated in the MG-63 cells compared to the other cell lines.

Conclusion: According to the findings of the study, the C3G is a novel anti-osteosarcoma agent with the ability to induce the apoptosis in different osteosarcoma cells through upregulation of the PPARγ and P21 genes.

Keywords: MTT; Osteosarcoma; P21; PPARγ; apoptosis; cyanidin 3-O-glucoside

Cytotoxic Effect of Simvastatin-loaded PCL-PEG nano-fiber scaffolds on 5-Fluorouracil-resistant MKN-45 Cell Lines of Gastric Cancer (Research Paper)

Elham Norouz Dolatabadi,[1] Vahid Asghariazar,[2] Maryam Darvish,[3] Kazem Nejati koshki,[4,*]

1. Biotechnology department, Arak university of medical sciences, Arak, Iran
2. Immunology research center, Ardabil university of medical sciences, Ardabil, Iran.
3. Biotechnology department, Arak university of medical sciences, Arak, Iran
4. Pharmaceutical Sciences Research Center, Ardabil University of Medical Sciences, Ardabil, Iran

Introduction: Gastric cancer (GC) is one of the most common and invasive cancers in humans. According to GLOBOCAN 2018 data, Stomach cancer is the 5th most prevalent neoplasm and the 3rd most lethal malignancy. 5-Fluorouracil (5-FU) is extensively used in cancer treatment. However, drug resistance remains a major hurdle to 5-FU's therapeutic application. Therefore, new studies focus on the use of combination therapy as a new method of overcoming drug resistance. 3-Hydroxy-3-methyl glutaryl-CoA reductase inhibitors, known as statins, are commonly used to treat hypercholesterolemia, but their effects have also been proven to treat cancer. Simvastatin, a member of the statins family, has been shown to have anti-proliferative and apoptotic effects via upregulating and maintaining p53 phosphorylation. Simvastatin is very sensitive to hydrolytic conditions. Therefore, their physical encapsulation inside PCL-PEG (polycaprolactone-polyethylene glycol) as a hydrophilic biocompatible material can be a suitable method for the effective use of hydrophobic statins in the pharmaceutical industry. Our aim is to evaluate the cytotoxic effect of Simvastatin-loaded PCL-PEG scaffolds on 5-fluorouracil-resistant MKN-45 cells in Gastric cancer

Methods: The human GC MKN-45 cell line was supplied from the Pasteur Institute of Iran. RPMI-1640 culture medium containing 10% FBS complemented with 1% Penicillin Streptomycin solution was utilized to culture MKN-45 cells. The cells were maintained in T25 cell culture flasks in an incubator at 37°C with high humidity (95%) and 5% CO2. Simvastatin-loaded PCL-PEG nano-fiber scaffolds were designed by electrospinning and characterized by SEM and FTIR imaging. The scaffolds were cut to size and placed on the plate after sterilization. MKN-45-resistant 5-fluorouracil cells were then cultured on them. After 3 and 7 days, MTT assay and imaging of scaffolds were performed to determine the rate of cell proliferation on the scaffold.

Results: The MTT assay was performed to determine the effect of Simvastatin-loaded PCL-PEG scaffolds on cell viability. MTT test showed a significant increase in cell killing activity of Simvastatin released from PCL-PEG scaffold on MKN-45 cells ($P < 0.05$). The results also show the time-dependent and dose-dependent effect of Simvastatin-loaded PCL-PEG scaffolds on 5-fluorouracil-resistant MKN-45 cells in Gastric cancer

Conclusion: The results of this study showed that Simvastatin loaded in PCL-PEG nano-fiber scaffold has the potential to inhibit proliferation and viability of 5-FU-resistant MKN-45 cell line. In addition, it can be concluded that Simvastatin loaded in PCL-PEG nano-fiber scaffold may be a suitable approach for combination therapy with drug 5-FU in Gastric cancer patients.

Keywords: Simvastatin, 5-Fluorouracil, PCL-PEG, Gastric cancer, Drug resistance

Deletion of PUF4 RNA-binding protein in Leishmania major through CRISPR/Cas9 technique (Research Paper)

Elaheh Davarpanah,[1] Tahereh Taheri,[2,*]

1. Department of Immunotherapy and Leishmania Vaccine Research, Pasteur Institute of Iran
2. Department of Immunotherapy and Leishmania Vaccine Research, Pasteur Institute of Iran

Introduction: Leishmaniasis is a neglected tropical disease that is caused by Leishmania (L.) parasites that transmits by the bite of infected sandflies. As a next generation of live vaccines, genetically attenuated parasites are more attention. PUFs are conserved RNA-binding proteins in eukaryotes that are responsible for regulation of RNA processing. Leishmania has 11 members of PUFs that lead to regulate gene expression post-transcriptionally. The main goal of this study is disruption of puf4 gene in L. major and generation an attenuated vaccine through CRISPR/Cas9 system.

Methods: In the first step, sgRNA and donor DNA primers have designed using different software (LeishGEdit, EuPaGDT, CCTop, CRISPOR and CHOPCHOP) to increase the accuracy of designed primers.

Results: Between 100 bp region from the beginning of the puf4 gene, four suitable sgRNA sequences (including: 5'- AAGACACAGGTGCAGATGCA-3', 5'-CAGCTCTTCGCTCTCGGATT-3', 5'-GCTCTCGGATTGGGCAAACA-3' and 5'-AGGTGCAGATGCACGGATGA-3') can be considered to have the highest efficiency in cutting the 5' of the puf4 gene. In addition, four appropriate sgRNAs for 3'-end cutting of gene have recognized (including: 5'-GCACGCATGCAAAATGCTAA-3', 5'-AGACGGAGCTCGCCTTGCTG-3', 5'-TAGTTGCGCGAGCTCAGCAG-3' and 5'-GACGGAGCTCGCCTTGCTGA-3'). GC content of primers is ranging from 33 to 64.8. In addition, to increase MMEJ (Microhomology-Mediated End Joining) rate and substitution of puf4 gene with antibiotic markers, two specific short nucleotide sequences (~30 nt) in upstream and downstream of the gene (5'-ACGTTGTGCAGCTCCCTTCACCGTCATCCG-3' and 5'-GAGTGCAGCGGCCGGGAACGGTGGCCACAC-3', with GC content 60% and 73%, respectively) have selected.

Conclusion: In the next step, sgRNA and donor DNA sequences will be used to create DSB within flanking puf4 target region and replace of two alleles with two drug resistance genes.

Keywords: Live vaccine, Leishmania major, PUF4, CRISPR/Cas9.

Design and construction of a universal payload vector for bxb1-based recombinase-mediated cassette exchange for targeting a transgene into a single locus in mammalian cell (Research Paper)

Samaneh Ghanbari,[1] Fatemeh Davami,[2,*]

1. Biotechnology Research Center, Pasteur Institute of Iran, Tehran, Iran
2. Biotechnology Research Center, Pasteur Institute of Iran, Tehran, Iran

Introduction: Chinese hamster ovary (CHO) cells are the most commonly used host for biotherapeutic production. The traditional method for stable cell line development is based on random integration of a gene of interest (GOI) which needs screening of several hundred clones to obtain high producer ones. With the advent of new genome-editing systems such as the CRISPR/Cas9 system, a new approach is toward site-specific integration which reduces clonal variation and accelerates the cell line development process. Recombinase mediated cassette exchange (RMCE) utilizes a site-specific recombinase/integrase which mediates recombination between its pre-integrated recognition site into a genomic site and its cognate attachment site on a transgene harboring vector (payload vector). It takes up to 12 months from transfection to lead clone cell banking in traditional cell line development. By using the CRISPR/Cas9 system in conjunction with RMCE technology (hybrid system), cell line development timelines can be significantly reduced to 4 weeks. In the hybrid system, CRISPR/Cas9 can be used to generate RMCE founder clone, a clone which contains a recombinase recognition site (attP site for bxb1 recombinase) in a specific locus. After characterization of the founder clone, it can be used repeatedly. In the presence of a recombinase vector, the landing pad of the founder clone is swapped for a therapeutic transgene using RMCE. To shorten the time frame even more, we have designed and constructed a universal payload vector with a multiple cloning site flanked by bxb1 recombinase recognition site (attB site). We also incorporated the Herpes Simplex Virus-1 thymidine kinase (HSV-TK) cDNA in the donor vector backbone to eliminate any possible random integration event following ganciclovir selection.

Methods: Construct design: Bx1 attB site sequence was obtained from literature review, to prevent unintended integration of plasmid backbone instead of donor cassette the multiple cloning site (MCS) flanked by inversely oriented attB sites (attB and attBi). Since orthogonal recombinase target site is needed in RMCE system, the cassette consist of MCS flanked in one side by bxb1 attB-GA mutant, and in the other side by the wild type one. To be able to clone HSV-TK cDNA, a cloning site was considered outside the attB sites. The designed construct was synthesized by Bio Basic Inc. (Markham, Ontario, Canada). HSV-TK cloning and transformation HSV-TK cassette together with its promoter PGK was PCR amplified from an in-house plasmid

using forward and reverse primers containing XbaI and KpnI site, respectively. XbaI/ KpnI digested PCR product was ligated into the XbaI/KpnI linearized payload vector. The ligation product was transformed into chemically competented E. Coli TOP10F´strain. Cloning confirmation Colony PCR was performed to screen colonies for the desired insert. The plasmid was extracted from a positive clone, digested with XbaI and KpnI, and analyzed by gel electrophoresis. Finally, the plasmid DNA was sent for sequencing (Macrogen, Korea).

Results: Schematic map of the designed plasmid containing attB-MCS-mutattBi and HSV-TK cassette is shown in Fig. 1. To verify cloning of PGK-TK into XbaI/KpnI site, resulting colonies were screened by colony PCR using forward primer on plasmid backbone and reverse primer on PGK construct leading to a 655 bp amplicon. Gel electrophoresis of PCR products shows 5 out of 5 clones were positive for cloning (Fig.2). An extracted plasmid from a positive clone was then digested with XbaI and KpnI. Fragments were verified by gel electrophoresis (Fig. 3).

Conclusion: In summary, we designed and constructed a universal payload vector to be used in CRISPR/cas9-RMCE hybrid system for targeted integration of a transgene into a defined locus in mammalian cells. By implementation of inversely oriented bxb1 attB sites, the possible integration of the vector backbone instead of the gene of interest has been eliminated. HSV-TK cassette on the vector backbone allows us to select transfected cell pool with ganciclovir resulting in a homogenous cell pool without random integrants. This ready-to-use payload vector only requires GOI cloning so reduces the time, burden and cost of multiple fragments cloning or synthesis.

Keywords: CRISPR/Cas9, recombinase-mediated cassette exchange, targeted integration, cell line development

Design and optimization of a real-time PCR assay for SARS Coronavirus-2 detection in stool sample (Research Paper)

Mobin Makhmalbaf,[1] Seyed Reza Mohebbi,[2,*] Seyed Masoud Hosseini,[3] Paria Pirasteh,[4] Shabnam Kazemian,[5] Hamid Asadzadeh-Aghdaei,[6]

1. 1 Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran -2. Department of Microbiology and Microbial Biotechnology, Faculty of Li
2. Research Center for Gastroenterology and Liver Diseases, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
4. Research Center for Gastroenterology and Liver Diseases, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
5. Research Center for Gastroenterology and Liver Diseases, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
6.

Introduction: The coronavirus disease 2019 (COVID-19) outbreak, which was caused by the novel SARS coronavirus 2 (SARS-CoV-2) in Wuhan, China, has spread around the world. Approximately 232 million cases of the disease and over 4.5 million COVID-19-related deaths have been announced worldwide. Due to the presence of SARS-CoV-2 in the COVID-19 patients' feces, it is really important to detect the viral RNA in stool samples of people suspected of the infection. Because of the high number of patients and the transmission ability of SARS-CoV-2, finding a fast, accurate and at the same time, low-cost assay to diagnose patients with COVID-19 is a major objective, especially in developing countries with limited resources and infrastructure. This study has developed a rapid, simple, and cost-effective diagnostic method based on SYBR green real-time PCR.

Methods: The viral RNA genome was extracted from stool samples, and cDNA was synthesized. Bioinformatics software was also used to design and analyze specific primers. The primers targeted a conserved region of the RdRP gene. A real-time polymerase chain reaction was performed and melt curves were analyzed. The results were compared with a commercial detection kit and also PCR and sequencing as a gold standard method.

Results: Twenty laboratory positive patient samples and twenty confirmed negative stool samples were used to evaluate the developed method. This

assay was also compared to commonly available kits with high sensitivity and specificity. After setting up, the target region was successfully amplified and detected with appropriate efficiency and reproducibility.

Conclusion: Given the significant prevalence of SARS-CoV-2 in the feces of COVID-19 patients, it is important to monitor stool samples of suspected people. We developed a method for all SARS-CoV-2 variants based on the results, which can be used as a proper diagnostic test for different SARS-CoV-2 variants.

Keywords: SARS-CoV-2 ,COVID-19 ,Real-time PCR, Primer design

Design and preparation of chitosan nanoparticles conjugated with LysK bacteriophage chimeric endolysine as a novel bacterial antibiotic (Research Paper)

Paria Abbasi,[1] Sepideh Khaleghi,[2,*] Hossein Fahimi,[3]

1. Department of Biotechnology, Faculty of Advanced Science and Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.
2. Department of Biotechnology, Faculty of Advanced Science and Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.
3. Department of Genetics, Faculty of Advanced Science and Technology, Tehran Medical Science, Islamic Azad University, Tehran, Iran.

Introduction: In recent years, resistance to antimicrobial drugs has become a growing global concern. To solve this problem, efficient solutions such as the use of nanomaterial such as chitosan nanoparticles with unique physicochemical properties and the use of chimeric endolysin protein derived from bacteriophage have been used. In this project, the aim is to synthesize chitosan nanoparticles to which the said peptide antibiotic is attached with covalent and non-covalent junctions

Methods: In this project, plasmid pET32 will be used to increase the expression, solubility, and proper folding of chimeric endolaysin protein. The expression of recombinant protein was improved by different culture conditions and purified with Ni-NTA column. Chitosan nanoparticles attached covalently and noncovalently with chimeric endolysine protein will be synthesized using Ionic gelation method. The physical properties and morphology of nanoparticles will be investigated with a TEM, DLS and FT-IR. Finally, the antibacterial effect of nanoparticles were evaluated against Pseudomonas aeruginosa, methicillin-resistant Staphylococcus aurous and Escherichia coli by MIC / MBC, biofilm and synergistic effect with vancomycin.

Results: Protein expression was improved in TB medium. Covalent of nanoparticles with endolysin chimeric protein by FTIR method showed that covalent bindings were performed correctly in a certain range and TEM electron microscopy showed that the nanoparticles were monodispersed and spherical. antibacterial experiments showed that the MIC / MBC assay had a positive effect of nanoparticles on all three bacteria at a concentration of 8ng/ml in 24 to 48 hours, but in the biofilm assay, it only affected Escherichia coli and did not cause biofilm formation. The synergy assay also affected three bacteria in CS-ChAmc (NC) treatment mode in 48 hours, but the most effect was observed on Pseudomonas aeruginosa in CS-ChAmc (NC) treatment mode

Conclusion: The chitosan nanoparticles conjugated with chimeric endolysin covalently and non-covalently can be an effective novel antibiotic against common infections.

Keywords: chitosan nanoparticles, Protein antibiotics, LysK, Bacteriophage

Design and synthesis of antifungal chitosan – albumin conjugated nano particle containing fluconazole (Research Paper)

Morvarid Hatamiazar,[1,*] Javad MohammadNejad,[2] Sepideh Khaleghi,[3]

1. Department of Biotechnology, Faculty of Advanced Science and Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.
2. Department of Life Science Engineering, Faculty of New Sciences & Technologies, University of Tehran, Tehran, Iran.
3. Department of Biotechnology, Faculty of Advanced Science and Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.

Introduction: Introduction: Candida species are the most common causative agents responsible for the majority of morbidity as well as mortality rates due to invasive fungal infections worldwide. The most candidiasis infection is Vulvovaginal candidiasis (VVC) that represents a considerable health burden for women. Despite the availability of a significant array of antifungal drugs and topical products, the management of the infection is not always effective, Fluconazole (Flu) is an antifungal frequently used in the treatment of mycosis and some fungi developed resistance to its mechanism of action, therefore new approaches are needed. Novel vaginal drug delivery systems can be used to provide local treatment. Vaginal drug delivery systems prevent systemic side effects and can provide long-term drug release in the vaginal area. Chitosan (CS) is a naturally originating product that can be applied in many areas due to its biocompatibility, biodegradability, and nontoxic properties. The broad-spectrum antimicrobial activity of CS offers great commercial potential for this product. Nevertheless, the antimicrobial activity of CS varies, because this activity is associated with its physicochemical characteristics and depends on the type of microorganism.

Methods: Methods: In this article Chitosan coated by Bovine serum albumin (BSA) with covalent (with EDC and NHS) and non-covalent bond and trapping fluconazole with ratios 1Flu:1CS , 1Flu:2CS and 2Flu:1CS in this nanoparticle , The physicochemical characterizations of biosynthesized CS-BSA -NPs were assessed by using Fourier transform infrared (FT-IR) spectroscopy, transmission electron microscope (TEM), scanning electron microscope (SEM), dynamic light scattering (DLS) Analysis. FT-IR analysis confirmed the presence of functional groups related to reduction, capping, and stabilizing CS-BSA-NPs. The MIC/MFC was assayed for the antifungal effect of nanoparticles. Moreover, the effect of nanoparticles was evaluated on biofilm formation.

Results: Results and Discussion: The DLS analysis showed that NPs were homogenous and monodispersed. The TEM and SEM showed spherical, nano sized nanparticles. The FT-IR conformed the covalent and non-covalent

bonds in samples. The recorded minimum inhibitory concentration (MIC) was18 µl/ml and minimum fungal concentration (MFC) was 22.5 µl/ml (1fluconazole:2CS-BSA–nanoparticle). CS-BSA nanoparticle has profound effect on biofilm formation. The cell viability assay (MTT) on human normal fibroblast cell lines showed biocompatibility of complex in 24h and 48h.

Conclusion: Conclusion: synthesized CS-BSA-NPs containing Fluconazole can be used as effective antifungal, biocompatible nano complex for Candida spp. 1. Facchinatto WM, Galante J, Mesquita L, Silva DS, Dos Santos DM, Moraes TB, et al. Clotrimazole-loaded N-(2-hydroxy)-propyl-3-trimethylammonium, O-palmitoyl chitosan nanoparticles for topical treatment of vulvovaginal candidiasis. Acta biomaterialia. 2021;125:312-21. 2. Soliman AM, Abdel-Latif W, Shehata IH, Fouda A, Abdo AM, Ahmed YM. Green approach to overcome the resistance pattern of Candida spp. using biosynthesized silver nanoparticles fabricated by Penicillium chrysogenum F9. Biological Trace Element Research. 2021;199:800-11. 3. da Silva JT, de Oliveira MG, de Paula JR, Alves SF, Pellegrini F, Amaral AC. HPLC Method Validated for Quantification of Fluconazole Co-Encapsulated with Propolis Within Chitosan Nanoparticles. Indian Journal of Microbiology. 2021:1-6. 4. Ke C-L, Deng F-S, Chuang C-Y, Lin C-H. Antimicrobial Actions and Applications of Chitosan. Polymers. 2021;13(6):904. 5. Tuğcu-Demiröz F, Saar S, Kara AA, Yıldız A, Tunçel E, Acartürk F. Development and characterization of chitosan nanoparticles loaded nanofiber hybrid system for vaginal controlled release of benzydamine. European Journal of Pharmaceutical Sciences. 2021;161:105801.

Keywords: Keywords: vulvovaginal candida;Fluconazole;Bovine Serum Albumin; nano particle; Chitosan;anti fungal

Design efficient RNAi sequences to postpone the metastasis by down-regulating ZEB1 in pancreatic cancer (Research Paper)

Mahbod Djamshidi,[1,*] Ghazal Mohammadbeigi,[2]

1. Department of Biology, Faculty of Science, University of Guilan
2. Department of Biology, Faculty of Science, University of Guilan

Introduction: The pancreas is a gland that produces chemical substances for food digestion (the exocrine component) and hormones (the endocrine component) that can give the creatures a helping hand to control the rate of sugar in blood [15]. Cancer is known as a heterogeneous disease, which is regulated by complex mechanisms that could promote both tumor initiation and progression [1]. In pancreas cancer, normal cells undergo stopping work and grow out of control to form a mass named tumor [15]. Cancer is a leading cause of death universally. Pancreatic cancer has given rise to 4.2% deaths in males and 4.9% in females in 2018 [1]. 1.2. Metastasis Most of the cancer deaths are caused by “metastasis” which means the spread of primary cancer to distant sites [2]. In other words, metastasis is the circulating of cancer cells via the vascular system and its establishment in a new location causing a secondary tumor. For many types of cancers, metastasis is also called stage IV (4) cancer or advanced cancer [2,3,15]. Clinically, it is diagnosed when observing cancer cells under a microscope having features like primary cancer cells but not resembled to the cells of the tissue they have found [2]. Cancer can spread to different sites. For example, in our case “pancreatic cancer”, tends to spread to the liver, lung, and peritoneum [2]. Treat metastatic cancer is hard and depends on cancer’s origin (where it started), the much of the spread, health, age, and some other things. Often the goal of treating metastatic cancer is to control it by stopping or slowing its growth.[3] Main types of treatment for metastasis are: • Systemic therapy: treatment affects the entire body including chemotherapy, hormone therapy, targeted therapy and immunotherapy. • Local therapy: treatment for the area with cancer including surgery, radiation therapy, and some other treatments. Metastasis has some steps which are demonstrated bellow in order [2,4]: 1. Invasion: growing into, or invading nearby normal tissues 2. Intravasation: moving through the walls of nearby lymph nodes or blood vessels 3. Survival: traveling through the lymphatic system and bloodstream to other parts of the body and survival within blood 4. Arrest: stopping in small blood vessels at a distant location 5. Extravasation: invading via blood vessel walls (hematogenous spread), and moving into the surrounding tissue like lung, liver, bone etc. (2way: first, moving through the blood vessel and second, cell gathering in capillaries till erupting the vessel) 6. Microenvironment: growing in target tissue until a tiny tumor form by resisting the target tissue ECM 7. Metastatic Colonization (MC): causing new blood vessels to grow, which creates a blood supply that allows the metastatic tumor to continue growing

Initiation of metastasis depends on invasion. A method that could suppress invasion can be a way to postpone metastasis. This may happen by suppressing effective signals and factors in invasion so it's important to know about invasions incidents. 1.3. Metastasis and Invasion Invasion is the mechanism by which affected cells penetrate into neighboring tissues [5]. As can be discovered in the following figure, metastasis and invasion are different mechanisms. Invasion refers to the ability of a tumor to expand into surrounding tissues while metastasis refers to the ability to penetrate into new tissue or distal organ at a different location [5]. The main process of invasion is penetration but metastasis, includes invasion, intravasation, and extravasation so invasion is a part of metastasis [5]. During the invasion in cancer progression, a variety of tumor cells show alterations in their plasticity by morphological and phenotypical conversions, including the epithelial to mesenchymal transition (EMT) so it is obvious that EMT initiates metastatic cascade [1] [6,12,]. 1.4. EMT EMT is a biologic process that allows a polarized epithelial cell to undergo multiple biochemical changes that enable it to assume a mesenchymal cell phenotype, which involves enhanced migratory capacity, remodeling of the cytoskeleton, the disruption of cell-cell adhesion and cellular polarity, invasiveness, elevated resistance to apoptosis and greatly increased production of ECM components [7,12-16]. EMT is a normal cellular process that regulates embryogenesis, tissue regeneration, organ fibrosis, and wound healing [1] [7-11,13,]. Metastatic tumor cells with a mesenchymal phenotype are believed to undergo a reverse transition (MET) that facilitates metastatic colonization at the site of metastasis to gain the pathology of their corresponding primary tumors by disseminated tumor cells [10,12]. As mentioned, the induction of EMT in epithelial cancer cells promotes migration, invasion, and dissemination [10]. There are three types of EMT [7,10]: • Type I: EMT during implantation, embryogenesis and organ development • Type II: EMT associated with tissue regeneration and organ fibrosis • Type III: EMT associated with cancer progression and metastasis The activation of tumor EMT typically occurs during signal swaps between tumor cells and adjacent stromal cells [8]. One hallmark of EMT is the downregulation or even loss of epithelial (E-)cadherin, which is an essential component of adherence junctions [6]. The subsequent upregulation of mesenchymal markers such as vimentin and neuronal (N-)cadherin is one of the hallmarks for mesenchymal cells [6]. This shift from E- to N-cadherin expression, termed cadherin-switch, leads to enhanced motility of EMT-transformed cells [6]. Initiate an EMT and orchestrating it triggered by complex regulatory networks including some transcription factors (EMT-TFs), such as the Snail, Twist, and ZEB families and some other things like expression of specific cell-surface proteins, reorganization and expression of cytoskeletal proteins, production of ECM-degrading enzymes, and changes in the expression of specific microRNAs (such as the miR-200 family, miR-205 and miR-9) [1][7,10,13,]. The complex regulatory networks facilitate EMT by downregulating epithelial genes (such as E-cadherin) and upregulating

mesenchymal genes. [1] 1.5. EMT regulation As EMT-TFs can down-regulate the metastasis-suppressor protein (E-cadherin) and up-regulate mesenchymal phenotype, it's expected that consumption and down-regulating of these TFs may postpone metastasis and inhibit the metastatic dissemination. All of these factors and their relations are available in the figure 1. 1) Snail: The Snail family includes Snail1, Snail2 (Slug), and Snail3 (Smuc) [8,9]. These factors regulate epithelial and mesenchymal markers [8,9]. Snail and Slug, as two master regulators of the epithelial-mesenchymal transition, mainly mediate E-cadherin repression and are overexpressed in cancer cells during EMT [9]. 2) Twist: Twist factor induces EMT by influencing other EMT-ATFs and contains two proteins (Twist1 and Twist2) [8,9]. These factors are absent in normal epithelium but are induced in many human carcinomas [8]. Usually, Twist is identified as Twist1 and Twist1 is thought more significant in cancer metastasis than Twist2 [9]. Twist1 represses E-cadherin by inducing Snail1 or Snail2 and then binding to its promoter so it decreases E-cadherins transcription indirectly [8,14]. Twist1 and Twist2 are upregulated at the invasive front of carcinomas in cancer and stromal cells [8]. 3) ZEB: The zinc finger enhanced binding (ZEB1(also known as TCF8 and δEF1) [10,11] and ZEB2(also known as SIP1) [11,14]) transcription factors inhibit the miR-200 family at the transcriptional level, whereas these miRNAs themselves post-transcriptionally repress the EMT-inducers ZEB1/2 [6,14]. ZEB induces EMT by inhibiting various epithelial genes [8,10,14] and can initiate stem cell properties by upregulation of Klf4, Sox2 and Bmi1 which are normally repressed by the miR-200 family [6]. ZEB1 can repress E-cadherin expression and reciprocally repress the expression of the miR200s so the EMT process would be resulted and tumorgenicity would be enhanced [11,14]. 4) miRNAs: MiRNAs play an important role in controlling tumor growth and progression. Some miRNAs function as oncogenes and tumor suppressors [8]. The miR-200 family including miR-200a, miR-200b, miR-200c, miR-429 and miR-141 leads to epithelial differentiation [8,14]. The mechanism of miR-200s suppress ZEB1 so they would be used as a cancer treatment [11]. These microRNAs work in concert to repress EMT by targeting ZEB1 and ZEB2, which are direct repressors of E-cadherin. ZEB1 and ZEB2 also transcriptionally repress miR-200c in a double-negative feedback loop, facilitating the maintenance of a mesenchymal state [11,14]. Interestingly, the knockdown of ZEB1 in mesenchymal-like pancreatic cancer cell lines reversed the EMT phenotype [10]. Snail, Twist, and ZEB1 can enhance invasion and promote the degradation of E-cadherin [8,14]. Zeb1 can directly bind to specific DNA sequences named E-boxes (the gene encoding E-cadherin) and drive EMT and caner progression [10]. Expression of ZEB1 correlates with loss of E-cadherin (downregulation) [9,14]. The expression of both ZEB1 and ZEB2 is regulated by Snail1 in certain contexts, and Snail2 activates ZEB1 by directly binding to its promoter [14]. The aberrant expression of ZEB1 is thought to be connected with tumorigenesis and poor prognosis in various tumors, especially in breast cancer [11]. Other transcription factors also induce EMT

and tumor invasiveness. The homeobox factor goosecoid induces EMT by activating mesenchymal genes and repressing epithelial markers [8]. The growth factor TGF-β induces goosecoid in breast epithelial cells, and goosecoid is overexpressed in ductal breast carcinomas and atypical ductal hyperplasia [8]. It is directly activated by hypoxia via hypoxia-inducible factor 1 alpha (HIF1α) [14]. HIF1α can also induce epigenetic regulation of EMT by transcriptionally targeting HDAC3, which cooperates with the EMT-associated TF Snail1 to mediate gene repression of epithelial-specific promoters [14]. TGF-β is an important suppressor of epithelial cells [15]. It stimulates cells to lose epithelial markers, such as E-cadherin, and also to gain mesenchymal markers, such as vimentin. TGF-β is related to cell proliferation, and when this growth factor is mutated, it contributes to the uncontrolled proliferation of cancer cells [15]. 2. Aim This article will focus on the EMT transcription factor “ZEB1” and its correlation with stemness-repressor miRNAs to design a siRNA to inhibit this EMT-TF and postpone the metastasis of cancer.

Methods: 1. NCBI [16] used to identify special sequences and their homology in comparison with other resembled ones. 2. Gene-Runner exploited to predict Hairpin loops, Dimers, Bulge loops, and match sites in a given sequence’s binding site. 3. RNA Central [17] utilized to confirm the NCBI data by using 3-dimensional graphs and certified information 4. IDT Oligo Analyzer [18] used to recheck Gene-runner’s data’s accuracy 5. RNA Fold [19] utilized to be aware of the binding location’s both specificity and entropy that culminated in binding affinity. 6. Zincdb, Bindingdb and Drugdb [24-26] used as resources of official and existed ligands.

Results: 3.1. It was assumed that Zinc Finger E-box Binding homeobox 1 [Homo sapiens] has 44 significant transcripts, which are all protein-coding mRNAs. ZEB1 transcript variant 1 that contains 6192bp, not only is known as the longest transcript variant of the ZEB1 gene (Location: 10p11 .22, Exon count; 20) but also covers all other variants of the gene transcripts at least on 91% in transcript variant 25 and the most on 100% in transcript variant 7. [16] Moreover, all these data rechecked by RNA central and proved with same results. [17] 3.2. Ten significant RNAis, which are available in chart 3.1 are designed by Gene Runner computer-based engine concerning highly-effective siRNA guideline. [20] Firstly, these sequences are analyzed by the oligo analyze tool in the application. How calculations illustrate the condition; all sequences checked by their attributes and potential in making secondary structures such as Hairpin loops, Dimers, Bulge loops, and match sites. Furthermore, the sequences were rechecked and revised with a more powerful engine, which is known as the IDT analyzer tool. [18] A few novel characteristics were found out in the new results and the estimated Tm was a bit different (this difference is based on diverse Tm methods that are used by these analyzers) from the former. 3.3. In addition, the specificity of designed RNAis blasted by the NCBI BLAST tool separately. Results depict that three

substantial RNAis have non-specific binding to other mRNAs based on Nucleotide Collection (nt) database. Therefore, all these three sequences, which are specified in the figure by red color, were eliminated and the study continued with the other distinguished RNAis. 3.4. Besides, these remained RNAis checked for binding and entropy potential according to data is achieved from RNAfold Webserver diversely. [19] The results are based on base-pair capability and second structure occurrence capability. 3.5. Finally, a common 5'- TCAAGAG-3' hairpin was added in the middle of the sequence to prepare the most effective mature RNAi structures, which are predicted in this study for injecting into the cell for more in vivo/in vitro experiments. The ultimate results, which are rosed from our filters that were elaborated before in the article, are available in chart 3.2. In the current study, we focused on optimizing novel RNAis based on any accessible feature to increase the efficiency of deactivating all ZEB1 transcripts, which over-expressed in an astonishing number of pancreatic cancers patients. Unfortunately, many of the cases with signs of the over-expression of ZEB1 and consequently, the lack of E-cadherin as one of the main characters in cell-to-cell connection. This circumstance, will promote the metastasis process and lead patients to die.

Conclusion: Whereas ZEB1 plays a critical role in metastatic cell specially in the preparation process of EMT, it would be both beneficial and practical to cut the cascade as early as feasible or in crucial points; therefore, ZEB1 was chosen because of its unique characteristics. According to bindingdb [24], drug bank [25] and Zincdb [26], there is no official and specific ligand to inhibit ZEB1 as main vertex in the network of many of the effective elements in EMT process such as Twist, Snail, Slug, miR-200, miR-205 and SOX family. In other words, if there is any specific ligand to down-regulate the over-expressed ZEB1 in pre-EMT condition. Here, we suggested a number of RNAi sequences to inhibit the over-expressed ZEB1 in pancreatic tumor cell expeditiously as our first step in the full study in this case. In this research, we designed several specific RNAis with an optimized format by using the strongest engines in each part. We also used different well-known protocols to optimize many parameters such as Tm, length, starting nucleotide, GC content, selected region, and thermodynamic properties. All of these, besides to target's entropy and binding probability, support our results fidelity. In the next step, we will check to be aware of the exact rate of the RNAis' efficiency. We hope that our outcome will be used as the first official, a specific and effective nucleotide-based ligand to postpone EMT and subsequently, metastasis in cancer patients besides to other discovered drugs. Of course, new approaches in the drug delivery field can increase the effect of our RNAis. What is your perspective about this notion? "We are going to use accurate nucleotide treatments to reduce side effects and many problems that common drugs have." If you are interested in this field of study, you can check these useful references for further information. [21]-[23]

Keywords: Cancer RNAi Pancreatic ZEB1 Metastasis

Designing a live vaccine against cutaneous leishmaniasis encoding sandfly salivary proteins and T2A peptide by immunoinformatics and homology modeling (Research Paper)

Mahya Sadat Lajevardi,[1] Tahereh Taheri,[2] Elham Gholami,[3] Negar Seyed,[4] Sima Rafati,[5,*]

1. department of Immunotherapy and Leishmania Vaccine Research, Pasteur Institute of Iran, Tehran, Iran
2. department of Immunotherapy and Leishmania Vaccine Research, Pasteur Institute of Iran, Tehran, Iran
3. department of Immunotherapy and Leishmania Vaccine Research, Pasteur Institute of Iran, Tehran, Iran
4. department of Immunotherapy and Leishmania Vaccine Research, Pasteur Institute of Iran, Tehran, Iran
5. department of Immunotherapy and Leishmania Vaccine Research, Pasteur Institute of Iran, Tehran, Iran

Introduction: Intracellular parasites of the Leishmania genus are deposited in the host skin through sandfly bite along with sandfly saliva. Salivary proteins alone or in combination with parasitic antigens are promising candidates for vaccine formulation against Leishmaniasis. Herein, two immunogenic salivary proteins (PpSP15 from Ph. papatasi and PsSP9 from Ph. sergenti) were analyzed at RNA and protein level for the best combination with or without the linker to be further cloned in L. tarentolae as a live vaccine.

Methods: All possible combinations of PsSP9 and PpSP15 with or without T2A linker (PpSP15-T2A-Ppsp9, PpSP9-T2A-Ppsp15, PpSP15-Ppsp9, and PpSP9-Ppsp15) were designed at mRNA and protein levels. At the mRNA level, the transcript synthesized in L. tarentolae was estimated using trans-splicing. Then, the secondary structures of the mRNAs were predicted by the RNAfold web server. At the protein level, the 3D models of all combinations were generated by I-TASSER and refined by GalaxyRefine servers, and then validated by different parameters. Validated models were superimposed to original proteins using UCSF Chimera. The combined structures were also further analyzed for junctional T-cell epitopes and population coverage of the selected vaccine construct by immunoinformatics. The vaccine candidate was selected based on mRNA and protein stability results besides peptide analysis and physicochemical properties were qualified by ProtParam.

Results: At the mRNA level, the most favored secondary structure was PpSP15-T2A-PsSp9. At the protein level, all refined 3D models of the four combinations were structurally valid however local quality estimation showed that PpSp15-T2A-PsSP9 fusion had higher stability for each amino acid position with high superimposition quality to both original proteins. Local

quality estimation of dissociated proteins followed T2A auto-cleavage (PpSP15-T2A and PsSp9-His tag) also indicated that T2A sequence or His-tag at the C-terminus of dissociated components neither affects the superimposition result nor generates new junctional epitope. The selected combination (PpSP15-T2A-PssP9) and the 2 resulting proteins (PpSP15-T2A and PpSP9-His-tag) were hydrophobe, immunogen, non-allergen and stable. Stable cloning of the selected combination in L. tarentolae resulted in successful protein production.

Conclusion: Immunogenic proteins from sandfly saliva can be successfully combined with virus-derived self-cleaving 2A peptides for live vaccine development.

Keywords: Cutaneous leishmaniasis, Vaccine, Homology modeling, sandfly saliva

Detection of salivary biomarkers 2D-carbon biosensors (Review)

Fereshteh Gholami,[1] Amin Hajhosseini,[2] Fatemeh Fathi Tadavani,[3] Maryam Mosallanejad,[4] Seyyed Ebrahim Moosavifard,[5,*]

1. Student Research Committee, Bushehr University of Medical Sciences, Bushehr, Iran
2. Student Research Committee, Bushehr University of Medical Sciences, Bushehr, Iran
3. Student Research Committee, Jahrom university of medical sciences, Jahrom, Iran
4. Department of Exercise Physiology, Faculty of Physical Education and Sport Sciences, Shahid Bahonar University of Kerman, Kerman, Iran
5. Seyyed Ebrahim Moosavifard, Department of Advanced Medical Sciences & Technologies, School of Medicine, Jahrom University of Medical Sciences, Jahrom, Iran

Introduction: The secretion of natural fluids in various parts of the body, including saliva, helps to examine and identify specific analytes. Saliva is a mucosal substance that contains mucin, amylase and various ions that have been used as an important diagnostic material in recent years due to easy access and cost-effectiveness, different analytes, non-invasiveness, high water content and rapid sampling capability. Due to these features, saliva sampling is an easy and safe process and allows continuous control and sampling. The manufacture and design of carbon-based biosensors for detecting salivary biomarkers will lead to the diagnosis and prevention of various diseases and improve the health of individuals. Biosensors are a type of chemical sensor that can convert chemical information into a signal by colliding with biological materials. The use of carbon material in the design of biosensors has been considered for many years. Graphene as one of the most attractive 2D carbon material has special and unique properties, and It has high electrical and fluorescence properties and is therefore one of the most widely used and valuable nanomaterials in the field of biosensors. The aim of this study was to investigate different types of 2D carbon-based biosensors to identify salivary biomarkers.

Methods: In the forthcoming systematic study, the required data were collected using 5 keywords including saliva, biomarkers, 2D carbon, graphene as well as biosensors and citing valid databases such as: Scopus , PubMed, Google Scholar and ProQuest. The statistical population of the study includes all studies conducted up to 2021 in the field of carbon-based biosensors for salivary biomarker detection. After reviewing the relevant findings and evaluating the data quality, a total of 20 articles were analyzed.

Results: In this systematic review, various types of salivary biomarkers of 2D-carbon biosensors have been introduced. The first biosensor is based on a reduced graphene oxide (RGO) and is supplemented with zirconia. This biosensor is used to detect the amount of CYFRA-21-1 in saliva. It can be also used to diagnose cervical cancer. In the next biosensor, the signals are amplified using poly-HRP-streptavidin compounds. Double-walled carbon nanotubes are used to make this type of biomarker. In this procedure, p-aminobenzoic acid is used to identify tumors such as necrosis tumor α and Interleukin 1 β those in spiked serum and saliva. The next biosensor is a graphene-based non-enzymatic ammetric sensor that is used to determine the concentration of glucose in saliva. In the next sensor, a neural sensor was designed to measure the DJ-1 protein using multiwalled carbon nanotubes, gold nanoparticles and composites. The cover of this sensor is made of polyethylene terephthalate. The amount of this protein in saliva and cerebrospinal fluid is very important. This sensor can be used in diseases such as Parkinson's.

Conclusion: In this review study, we examined 2D carbon-based biosensors. The use of salivary biomarkers detection is a cost-effective, non-invasive and accessible way to control health and prevent and diagnose various diseases. For example, an amp sensor that detects glucose concentration is non-enzymatic and is a fast and effective way to detect glucose levels. Despite the high advantages of saliva compared to other secretions, the possibility of changes in saliva composition and lower concentration of its analytes compared to some secretions is one of the disadvantages of saliva. Therefore, the development of research related to graphene-based salivary sensors will greatly contribute to the further development of this field and the elimination of the defects and shortcomings of these sensors.

Keywords: Saliva, biomarkers, 2D carbon, graphene, biosensors

Determination of Frequency of Human Papillomavirus Infection and it's genotypes among Patients with Prostate Cancer in Bushehr Province, 2010-2018 (Research Paper)

Fatemeh Farshadpour,[1] Reza Taherkhani,[2,*]

1. Department of Virology, School of Medicine, Bushehr University of Medical Sciences
2. Department of Virology, School of Medicine, Bushehr University of Medical Sciences

Introduction: Background and aims: Prostate cancer is one of the most important malignant tumors in men and is the second common cancer among men throughout the world. The role of infectious agents and oncoviruses such as human papillomaviruses in contaminating prostate regions, which can occur as a result of dissemination from contaminated anogenital areas or through blood or lymph, is mentioned as a potential risk factor for prostate cancer. This study was conducted to determine the prevalence and genotype distribution of human papillomavirus in paraffin-embedded tissue specimens from patients with prostate cancer in an 8-year period in Bushehr province using nested-PCR technique.

Methods: Materials and Methods: This study is a descriptive cross-sectional study. The study population includes paraffin-embedded prostate specimens of patients with prostate cancer referred to the Shohadaie Khalij-Fars Hospital in Bushehr during 2010 to 2018. Cancerous paraffin-embedded tissue specimens from 49 patients and 170 non-cancerous paraffin-embedded tissue samples (Hyperplasia with and without inflammatory tissue specimens) as control group were investigated for nested PCR method. Data were analyzed using SPSS software, Chi-square and Fisher's statistical tests.

Results: Results: The mean age of 49 patients with prostate cancer, who were investigated in molecular analysis, was 73.2 ± 8.2 years (with age range from 50 to 85 years). Most of the patients were between the ages of 70-79 years and then over 80 years. Most cases of prostate cancer were from 2013. In terms of Gleason score, the highest prevalence of prostate carcinoma was with a Gleason score equal to and greater than 8, followed by Gleason score equal to and lower than 6. The overall prevalence of HPV infection in 49 malignant prostate cancer cases was 4.1% (2 cases). Out of 170 non-cancerous prostate tissue samples (control group), HPV infection was observed in two cases, and the overall prevalence of HPV in the control group was 1.2%.

Conclusion: Conclusion: The overall prevalence of HPV infection in adenocarcinoma prostate samples and in the control group was very low. In addition, there was no significant statistically relationship between age, city, year and types of malignant and benign prostate lesions with the prevalence of HPV infection (p value> 0.05). Therefore, the role of other risk factors for prostate cancer such as age, diet, genetic factors and environmental factors may be more important than the role of human papillomavirus in the development of prostate cancer.

Keywords: Human Papillomavirus, Prostate Cancer, Bushehr province, nested-PCR technique

Developing an improved method for generation of human T cell clones
(Research Paper)

Mahdie Jafari,[1] Mohammad Ali Shokrgozar,[2] Shahriyar Abdoli,[3] Masoud Moghaddam Pour,[4] Zahra Sharifzadeh,[5,*]

1. Immunology Department, Pasteur Institute of Iran, Tehran, Iran
2. National Cell bank of Iran, Pasteur Institute of Iran, Tehran, Iran
3. School of Advanced Medical Technologies, Golestan University of Medical Sciences, Gorgan, Iran
4. Scientific board of Zist Fanavaran Pajoh Alborz Company, R&D Departmen, Karaj, Iran
5. Immunology Department, Pasteur Institute of Iran, Tehran, Iran

Introduction: T cell-based immunotherapy is a promising treatment for cancer, human immunodeficiency virus infection/acquired immunodeficiency syndrome, and other diseases. Current immunotherapies, such as the generation of chimeric antigen receptor (CAR)-T cells or gene editing using clustered regularly interspaced short palindromic repeat (CRISPR) technology, often require the genetic manipulation of T cells. Peripheral blood T lymphocytes are a pool of cells with extremely different characteristics and, therefore, it may be difficult to obtain clear results and to attribute a certain function to a defined T cell population in several experimental settings. The availability of a population of human T lymphocytes deriving from the same progenitor with a unique phenotype and function (clone) may therefore be of help. At present, the isolation and growing of single cells is still a technically challenging task; especially in suspended cells used in a wide range of CAR T cell studies. Therefore, researchers are still trying to establish an easy and effective method for isolation and expansion of single T clones. In this regard, we aimed to develop a simple and cost-effective method to enable isolation of human T cells at high yields and viability.

Methods: In this study, we explored the factors affecting T cell growing and assessed their ability to develop homogeneous clone from a single cell. At first, single T cells were isolated by serial dilution and seeded in 96 cell plates. Different factors affecting cell growth and survival and factors increasing the interaction between cells to facilitate clone formation including FBS, Matrigel and feeder layer cells were selected for this project. These factors were used for T cell expansion, separately or simultaneously, in ten different groups. The microplate wells were coated with the defined factors and then single T cells were added. Every two to three days, about 20 microliters of medium containing 20% FBS was added to cells. All wells were examined for two weeks and the single clones were transferred to a new well and propagated.

Results: By examining the microscopic images of T cells in terms of morphology and comparing the survival of clones formed within the experimental groups, three groups of pre-coated wells with 300 µl FBS, 100 µl Matrigel and FBS-Matrigel showed the best results. Among them, wells coated with FBS and Matrigel for 48 and 3 hours, respectively, showed the best results after cell seeding and clone formation. The T cell clones developed in these wells were successfully transferred to the new wells and expanded.

Conclusion: Due to the cost-effectiveness of FBS compared to Matrigel and the simplicity of this method compared to feeder layer cells, as well as its easy and short-term preparation that can reduce the risk of contamination, this method can be considered as a simple and cost-effective method to isolate and expand T cell clones. This protocol can replace time-consuming and expensive methods for T cell expansion to address the challenges of T cell proliferation and cell line development.

Keywords: Chimeric Antigen Receptor, T cell clone expansion, single cell isolation, cancer immunotherapy, Limi

Development of a novel tetra-primer ARMS-PCR for the identification of hotspot mutation BRAF V600E in patients with melanoma and colorectal cancer (Research Paper)

Mehran Sepehriyan Bahary Nezhad,[1,*] Ali Nazemi,[2]

1. Department of Biology, Faculty of Biological Sciences, Islamic Azad University of Tonekabon, Tonekabon, Iran
2. Department of Biology, Faculty of Biological Sciences, Islamic Azad University of Tonekabon, Tonekabon, Iran

Introduction: The BRAF mutations contribute to different types of cancer, and BRAF mutation screening may provide an effective prognosis. Therefore, the present study aimed to develop tetra-primer amplification refractory mutation system-polymerase chain reaction (ARMS-PCR) for the rapid detection of BRAF V600E mutation in patients with melanoma and colorectal cancer (CRC).

Methods: The present study analyzed 10 deoxyribonucleic acid (DNA) samples extracted from patients' tissues were prepared from a laboratory in Tehran province. Five samples were from patients with melanoma, four of which had an unknown genotype, and one sample had a mutant genotype that was used as a positive control. The other 5 samples had an unknown genotype and were related to patients with colorectal cancer. The DNA samples were analyzed using tetra-primer ARMS-PCR for the presence of BRAF V600E mutations. After the determination of the optimal temperature and optimization of tetra-primer ARMS-PCR based on normal DNA, the main reaction was performed in a microtube.

Results: The analysis of PCR sequencing electropherogram confirmed the presence of BRAF V600E mutation (GTG>GAG) at position c.T1799A in the melanoma DNA sample. In addition, two (22.22%) out of nine unknown genotype DNA samples were BRAF V600E positive. In contrast to the negative control, the development of a sharp BRAF V600E band by positive control indicated the proper functioning of the system used in this study.

Conclusion: In summary, the results of the present study demonstrated that the method of tetra-primer ARMS-PCR is an effective approach for the identification of BRAF V600E mutations. meanwhile, developed primers in this study can detect V600A(GTG > GCG) and V600G(GTG > GGG) mutations in addition to V600E(GTG > GAG) mutation due to their novel design.

Keywords: Tetra-primer ARMS-PCR, BRAF, Cancer, Mutation

Diagnosis, treatment pathways and neurophysiology in Angelman syndrome. (Review)

Fatemeh Kharatnejad,[1,*]

1. Azad university of Dezful

Introduction: Angelman syndrome is a complex genetic neurological disorder that primarily affects the nervous system. It was first reported in 1965 by the English pediatrician Harry Angelman. Angelman syndrome is caused by a small deletion in the long arm of maternal chromosome 15, del15q11, q13. Angelman syndrome is caused by a mutation in the UBE3A gene. Mutations in this gene lead to the inactivation of the E6-AP protein, which is responsible for the synthesis of ubiquitin cell layers. In Angelman syndrome, about 4MB (4MB) is removed from the long arm of the mother chromosome 15, which In the biological processes of a DNA molecule, such a change is a major error.Nerve physiology in Angelman syndrome: One of the more striking features of Angelman syndrome is the neurophysiological parameters. Because the electroencephalogram (EEG) rate is very abnormal. There are three distinct neurological patterns on electroencephalogram in patients with Angelman syndrome: The first pattern is the 2-3 Hz range, which will lead to a sharp decrease in perceptual power. The second pattern, which is the most common pattern, is in the range of 4-6 HZ, which leads to growth retardation and lack of learning and education in patients. The third pattern - in the range of 3-6 HZ, which leads to intensified laughter and blinking at high speeds. However, the nerve cells of people with Angelman syndrome appear to be properly synthesized, but they may not function properly.Clinical signs of Angelman syndrome: Symptoms of the disease can be divided into three categories: fixed, common and accompanying. Fixed symptoms include severe developmental delay, speech disorder, movement or balance disorders (ataxia and tremor movements), specific behaviors, irritable personality, and lack of concentration. Common symptoms include microcephaly that begins before age 2 and seizures that usually begin under age 3, and electroencephalography. Accompanying symptoms include protruding tongue, flat back, frequent tongue protrusion, malnutrition in infants, spaced teeth, runny mouth, strabismus, hypopigmentation of the skin, increased deep tendon reflexes (DTR) in the lower extremities, disorders Sleep is fascinated and staring and is very sensitive to heat, seemingly happy behavior, occasional laughter, jumping movements and imbalance.Diagnosis based on observation of delay in general development and inability to express words and seizures and gait It is done rigidly. Genomic hybridization comparison technique (a CGH) is used to detect the deletion or non-deletion of UBE3A gene activity in the long arm of chromosome 15 of the mother. A combination of genetic tests can detect chromosomal defects related to the syndrome. ligation-dependent probe amplification (MLPA) can be

done.Treatment options: There is currently no cure for Angelman syndrome. But there are medications and ways to control the condition. The severity of epilepsy can be controlled with several types of anticonvulsants such as phenotoin, phenobarbital, sodium valproate, and mild laxatives to encourage regular bowel movements. Perform physiotherapy to prevent joint stiffness. And perform speech therapy and anticonvulsant use for patients with severe disease. Several clinical trials are underway for Angelman syndrome, but there is no definitive genetic treatment Does not exist.

Methods: by study and review articlrs

Results: At present, the treatment of this syndrome is symptomatic and supportive, and genetic therapy or medication There is no specific and it can be controlled only with a series of drugs and occupational therapies.

Conclusion: Due to a gene defect or lack of a gene called UBE3A, nerve cells in the brain of infected people do not work properly, which causes a range of mental and physical problems. This genetic disease is rare and affects one in every 15,000 to 20,000 people.

Keywords: Angelman syndrome, Neurophysiology, Chromosome 15, UBE3A gene,treatment

Differencial expression genes and ceRNA network by microarray analysis in the breast cancer samples (Research Paper)

Mehrnoush Rishehri,[1] Mohammad rezaei,[2] Mansoureh Azadeh,[3,*]

1. Zist Fanavari Novin Biotechnology Institute, Isfahan, Iran
2. Zist Fanavari Novin Biotechnology Institute, Isfahan, Iran
3. Zist Fanavari Novin Biotechnology Institute, Isfahan, Iran

Introduction: Colorectal cancer (CRC) is the third most common cancer, influencing both colon and rectum (large intestine) through aberrant cell proliferation. (Rad et al., 2020). Therefore, this study aimed to identify potential diagnostic markers for CRC (Xie et al.,2021). Among them aberrant expressions of lncRNAs, miRNAs showe the close correlations in occurrence, development of CRC (Tang et al., 2019).

Methods: Rawdata of GSE113513 dataset from NCBI Gene Expression Omnibus (GEO) was normalayzed via limma and affy packages of R programming and figures from up and down expression (DEGs) were drawn by pheatmap (Fig.1), ggplot2 (Fig.2) and gplots (Fig.3) packages in the micoarray analysis. In addition, mRNA has been chosen as differencial expression gene. Finally, mRNA can to establish a ceRNA network with microRNA and lncRNA using miRWalk2.0, LncRRIsearch-rtools V.1.00 and DIANA-LncBase V.2 databases.

Results: the GSE113513 microarray dataset was used to identify differentially expressed genes (DEGs) between fourteen pairs CRC tissues and noncancerous tissues based on GEO. SFN gene chose as differentially expressed gene, which can to establish a novel ceRNA network (LINC00319 - SFN - hsa-miR-661), that hsa-miR-661 and LINC00319 targeting SFN gene, and LINC00319 has interaction with hsa-miR-661.

Conclusion: In summary,this findings could be suggested a novel interactions among lncRNAs, miRNAs and mRNA for the candidate diagnostic and prognostic markers associated with CRC by bioinformatics analysis.

Keywords: ceRNA, RNA interaction, Bioinformatics, SFN, Microarray

Discovery of new marine biopharmaceutics, via proteomics (Research Paper)

Naghmeh Roohi-Shalmae,[1] Rezvan Mousavi Nadushan,[2,*]

1. Department of Marine Science, Faculty of Natural Resources and Environment, Science and Research Branch, Islamic Azad University, Tehran, Iran.
2. Department of Marine Science, Faculty of Natural Resources and Environment, Tehran North Branch, Islamic Azad University Tehran, Iran.

Introduction: At the moment, according to antibiotics resistance, finding new effective biopharmaceuticals seems unavoidable. So in this critical condition, antimicrobial proteome extracted from natural sources can be useful to overcome this challenge. So diverse kinds of organisms like marine organisms has been investigated for their immunological responses to find antimicrobial agents. Serpulids of the Persian Gulf are one of these organisms that we focused on it to find antibacterial peptides or proteins.

Methods: Accordingly, at first HPLC-purified fractions of the coelomic fluid of these organisms were collected and then antibacterial activities of HPLC-purified fractions were investigated against gram negative/positive bacteria, and were assessed by inhibitory kinetic assay, two HPLC-purified fractions; F11, and FPIXC, showed antibacterial activity against gram-negative bacteria. The nature of purified fractions, F11 was defined as protein band at MW of ca. 65 kDa but F23 demonstrated a heterogeneous character. Subsequently, the proteinous fraction of major fraction, F23, was isolated by anion exchange chromatography as FPIXC. Hemolysis and MTT assays were performed on Human Embryonic Kidney 293 (HEK-293) cells, to investigate in vitro toxicity of F11 and FPIXC. Then characterizations of candidates were followed by MALDI-TOF analyses for partial identification. Bioinformatics analyses were subsequently employed to find their homologs, also used for determining their roles.

Results: The antibacterial activity of F11 was estimated to be twofold of FPIXC against Aeromonas hydrophila and Escherichia coli. F11 and FPIXC demonstrated similar activities on Vibrio harveyi, and no activity on Staphylococcus aureus. The MW of FPIXC was 8.5 kDa also it was distinguished as a unique peptide. F11 as one of the qualitatively dominant pure proteinous fractions showed homology with albumin protein.

Conclusion: Finally, two low toxic antibacterial proteome including homologs of the albumin and one unique peptide, were explored as possible new antibiotic in medical microbiology.

Keywords: Antimicrobial; Polychaete; MALDI-TOF; Bioinformatics; Proteomics

Distribution of Virulence Genes of Streptococcus agalactiae isolated from Pregnant Women in Bushehr (Research Paper)

Somayyeh Gharibi,[1,*] Mahnaz Gholipour shahrak,[2] Fahimeh Tavakoli,[3] Saeed Tajbakhsh,[4] Abbas Yadegar,[5] Zeinab Asen,[6]

1. Department of Microbiology, School of Sciences, Kherad Institute of Higher Education, Bushehr, Iran
2. Department of Microbiology, School of Sciences, Kherad Institute of Higher Education, Bushehr, Iran
3. Department of Microbiology, School of Sciences, Kherad Institute of Higher Education, Bushehr, Iran
4. Department of Microbiology and Parasitology, School of Medicine, Bushehr University of Medical Sciences, Bushehr, Iran
5. Foodborne and Waterborne Diseases Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
6. Department of Microbiology, School of Sciences, Kherad Institute of Higher Education, Bushehr, Iran

Introduction: Streptococcus agalactiae, GBS, is an important pathogen in neonates and pregnant women that normally colonizes the vagina and opportunistically leads to invasive diseases. GBS included several pathogenic genes that expression is directly involved in the prognosis of disease, bacterial survival and invasion. The aim of this study was to evaluate the frequency of group B streptococcal pathogenesis genes by PCR in pregnant women in Bushehr. Material and Methods: In this cross-sectional descriptive study, 25 GBS-positive samples isolated from pregnant women aged 35-42 weeks of pregnancy were studied. After DNA extraction and ensuring its purity, PI-1, PI-2a, PI-2b, PGi, fbsB, lmb and scpB genes were examined through specific primers.

Methods: In this study, 25 GBS-positive samples isolated from pregnant women aged 35-42 weeks of pregnancy were studied. After DNA extraction and ensuring its purity, They were confirmed by a housekeeping gene primer, pgi by PCR, and then PI-1, PI-2a, PI-2b, fbsB, lmb and scpB genes were examined through specific primers.

Results: The presence of pgi gene as housekeeping gene was confirmed in all strains. The sCpB gene was positive in 9 samples (36%). PI-1, PI-2a and PI-2b genes were found in 19 samples (76%), 1 sample (4%) and 1 sample (4%), respectively. The prevalence of fbsB was positive in 100% of the samples and the prevalence of lmb was positive in 92% of the isolates. 17 samples (68%) had at least one type of PI-1 cell. In one case (4%) there was a combination of PI-1 / PI-2b and in one case (4%) there was a combination

of PI-1 / PI-2a, while 5 samples (20%) did not have any pilus genes. In 4 samples (16%) there were 4 pathogens and in 2 cases (8%) there were 5 sCpB / PI-1 / PI-2a / fbsB / lmb factors (except PGi). 15 cases (60%) carried 3 pathogens. The predominant gene profile was PI-1 /lmb / fbsB with a prevalence of 76%. The scpB+lmb interaction was seen in 36% of the strains.

Conclusion: This study showed that the prevalence of virulence genes among the existing strains is highly variable. However, the isolates evaluated in it may contain other known and unknown virulence genes. These genes may also be expressed differently in various populations. That is why more research needs to be done on the prevalence of more virulence genes in more pregnant women.

Keywords: Streptococcus agalactiae, GBS, Pregnant women, Virulence genes, PCR

DNA damage response and repair in osteosarcoma: Defects, regulation and therapeutic implications (Review)

Fatemeh Sadoughi,[1,*] Parisa Maleki Dana,[2] Zatollah Asemi,[3] Bahman Yousefi ,[4]

1. Research Center for Biochemistry and Nutrition in Metabolic Diseases, Kashan University of Medical Sciences, Kashan, I.R. Iran
2. Research Center for Biochemistry and Nutrition in Metabolic Diseases, Kashan University of Medical Sciences, Kashan, I.R. Iran
3. Research Center for Biochemistry and Nutrition in Metabolic Diseases, Kashan University of Medical Sciences, Kashan, I.R. Iran
4. Stem Cell Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Introduction: Osteosarcoma (OS) is the most common primary malignancy developing bones. This disease which predominantly is developed in the metaphysis of long bones is able to show invasion and systemic metastases. In the late 70s, the 5-year survival rate of patients with OS has been estimated to be approximately 20%. In recent years, by the aid of new therapeutic methods the 5-year survival rate of OS has been improved to 78% in patients with localized disease; However, metastatic or recurrent forms of the disease have kept their 20% survival rate. DNA damage response (DDR) is a sophisticated multistep process containing a diversity of proteins which are necessary for the survival of any cell and organism. DDR machinery is able to detect abundant DNA lesions and afterwards, inhibiting the cell cycle progression when these lesions are not repairable. DDR is involved in a line of diseases including cancer. In recent years, DDR inhibitors have gained great attention due to their potentials in offering novel therapeutic targets and improving the response of many cancers to either chemo- or radio-therapy.

Methods: Surveying different articles related to our subject by using several search engines like google scholar, PubMed, and Scopus. We have tried to gather the most recent studies about the roles of DDR ingredients in OS pathogenesis and how these ingredients can be targeted for therapeutic purposes.

Results: According to evidence, a diversity of DDR ingredients are involved in the pathogenesis of OS. For instance, MRN complex (including MRE11, NBS1, and RAD50), PARP1, γH2AX, ATR/CHK1, MDC1, ATM/CHK2, BRCA1, EXO1, RAD51, and RAD52 are some of these ingredients with significant roles in OS initiation, progression, and resistance to therapies. Furthermore, a majority of these proteins can be used as therapeutic targets in order to increase the response of OS cells to either chemo or radiotherapy. For instance, different PARP1 inhibitors like Olaparib and 3-aminobenzamide,

H2AX inhibitors like miR 328 3p and miR-138, CHK1 inhibitors like Prexasertib, ATR inhibitors like Berzosertib, and CHK2 inhibitors like miR-191 are approved to be effective on OS cells.

Conclusion: Taken together, a majority of DDR-related proteins and genes are involved in OS initiation and/or progression and thus, DDR ingredients are considered proper options for treating OS patients. the least advantages of utilizing DDR inhibitors for osteosarcoma treatment is chemo- and radio-sensitization and thus, DDR inhibition is a promising procedure for enhancing the survival rate and prognosis of this cancer in the coming years.

Keywords: DDR, osteosarcoma, chemo-resistance, radio-resistance, MRN, PARP1.

Doxorubicin and Trifolium Pratense L. (Red Clover) Extract Synergistically Inhibits Brain and Lung Metastasis in 4T1 Tumor-Bearing BALB/c Mice (Research Paper)

Mohsen Akbaribazm ,[1,*]

1. Fertility and Infertility Research Center, Health Technology Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran

Introduction: Trifolium pratense L. (Red clover - T. pratense) commonly consumed as a healthy beverage has been demonstrated to have various biological activities including antioxidant and anticancer effects. The aims of study were to investigate the anti-metastasis effects of doxorubicin (DOX) and T. pratense extract in 4T1 tumor-bearing BALB/c mice.

Methods: In this study, 56 female BALB/c mice were divided randomly into seven 4T1 groups (n=8/group) to receive DOX and T. pratense in 3 different doses (100, 200 and 400 mg/kg/d) for 35 days. On the 36th day, serum cytokines (IL-8 and IL-6) were measured. GATA-3 Immunohistochemical (IHC) staining for brain and lung, and also CK5/6 for tumors tissue were performed. Metastasis-related genes [matrix metalloproteinase-2 (MMP-2) and sirtuin-1 (SIRT-1)] expressions are also measured by the Real- Time PCR.

Results: Our results showed that the co-treatment of DOX and T. pratense improved the lung and brain stereological parameters (decreased the volume of metastatic tumors) and decreased the serum levels of inflammatory and mediators of metastasis cytokines (IL-8 and IL-6). DOX and T. pratense synergistically down-regulated the MMP-2 and up-regulated the SIRT-1 genes and also decreased the CK5/6 positive cells in tumor tissues and inhibited metastasis in GATA-3 positive cells into lung and brain.

Conclusion: Our results present the first evidence on the anti-metastasis effects of T. pratense hydroalcoholic extract synergistically with doxorubicin as demonstrated by in vivo 4T1 metastasis inhibition in BALB/c mice bearing orthotopic breast cancer tumors.

Keywords: Trifolium pratense L., GATA-3, Metastasis, Isoflavone, 4T1

Drug safety in children and infants: A review of the types of drug errors and their causes (Review)

samaneh chenari,[1,*] mohadese saffari,[2]

1. Student Research Committee, Semnan University of Medical Sciences, Semnan, Iran
2. Faculty of paramedical school, Semnan University of Medical Sciences, Semnan, Iran

Introduction: A large part of medical errors are medication errors. Recognition of medication errors, prevention and understanding of its causes is essential. These errors are also common in children and infants ward. The aim of this study was to investigate the types of medication errors and their causes in pediatric and neonatal wards.

Methods: This study is a review that was performed during the period (2015-2021), by searching in valid foreign databases like Scopus, google scholar, Pubmed with the English keywords "Medication Errors", "NICU", "Pediatrics", "Neonate", "Patient's safety", and performed in valid domestic databases with Persian keywords "medication errors", "neonatal intensive care unit", "children", "neonates" and "patient safety". In the first step, a total of 35 articles were found, and finally 15 articles (10 foreign articles and 5 internal articles) that were more in line with the subject and the purpose of the research were selected and studied and organized.

Results: Most studies have shown that medication errors are more likely in premature infants, injectable medications and night shifts. In several studies, it was mentioned that the most errors in prescribing injectable drugs are related to errors in injection speed, errors in drug calculations, errors in dose and time of prescription, and neglect of drug interactions. In three other studies, the prescription of the wrong dose by physicians, nurses' fatigue, and illegibility of physicians' signatures were cited as the most important causes of medication errors. In two studies, some other causes of medication errors such as large number of patients, lack of manpower, failure to review medication instructions and improper adjustment of infusion devices were emphasized. Also in one study, one of the causes of medication errors from the nurses' point of view was the lack of information about the types of errors and how to report them.

Conclusion: To reduce errors, errors should be fully reported along with their cause, then these causes should be thoroughly investigated and redoubled efforts should be made to eliminate it. It is suggested that the following methods be used: Raising nurses' awareness and holding retraining classes

related to pharmacological information and improving the educational process, clear instructions on how to report, encouraging nurses to report medication errors and positive response of nursing managers, increasing the number of nurses to the patient.

Keywords: medication error, children, infants, patient safety

Dysregulation of CCL5 in a ceRNA network promote T-cell prolymphocytic leukemia in the G alpha and interleukin 10 signaling pathway: integrated bioinformatics and system biology analysis

(Research Paper)

fatemeh tavakoli kia,[1] mohammad rezaei,[2] mansoureh azadeh,[3,*]

1. zist fanavari novin biotechnology institute, isfahan, iran
2. zist fanavari novin biotechnology institute, isfahan, iran
3. zist fanavari novin biotechnology institute, isfahan, iran

Introduction: T-cell prolymphocytic leukemia (T-PLL) is an extremely rare type of leukemia with a high mortality rate. This malignancy characterized by the out-of-control growth of mature T- lymphocytes.t-pll accounts for 2 % of mature lymphocytic leukemia in adults, commonly patients over 65. even so, T_PLL is more heterogeneous and includes a wide range of clinical, morphological, and molecular characteristics, which sometimes makes diagnosis difficult. recent treatments don't have satisfying progress thus we need new treatment and cure. The main aim of this study is to find the potential biomarker and pathway to diagnose the malignancy in early stage.

Methods: For the start , the suitable GSE(GSE147930), gene expression profile, has been extracted from NCBI Gene Expression Omnibus(GEO) and analyzed by R studio so as to show gene expression profile (fig.4) and determine the gene which features a significant up and down expression regulation (fig.5). Ccl5 gene has been chosen since of its critical up regulation in tpll cells (fig.6). Moreover, the Free Online prediction software miRWalk 3.0 has been used to discover related miRNAs for ccl5 . After that to find lncRNAs which associated with miRNAs, the experimental and predictive DIANA LncBase v.2 modules were utilized.

Results: Based on GSE147930 , 416 up and down regulated gene were determined. Ccl5 up regulated gene were selected among these ups and down which has a interaction in G Alpha signaling , class A/1 and interleukin 10 signaling pathway (fig.8-10). hsa-miR-150-5p, hsa-miR-3667-3p, hsa-miR-20a-5p and hsa-miR-335-3p miRNAs were extracted from miRWalk 3.0. in addition HCG11, HCG18, SNHG14, ZNF883 and CASC9 LncRNAs were sponged by these miRNAs that were extracted from experimental and predictive DIANA LncBase v.2 modules. As a result these miRNAs and lncRNAs can act as a ceRNA network which has a effect on ccl5 gene regulation

Conclusion: To sum up our result, the mentioned lncRNAs (HCG11, HCG18, SNHG14, ZNF883 and CASC9) in ceRNA network can be used as a ccl5

expression regulator in tpll by having a major effect on hsa-miR-150-5p, hsa-miR-3667-3p, hsa-miR-20a-5p and hsa-miR-335-3p miRNAs which end up affecting G Alpha signaling , class A/1 and interleukin 10 signaling pathway. All these events can promote tpll in T-cell. Thus, these finding could provide a new therapy method and diagnose the malignancy in early stage.

Keywords: bioinformatics, microarray, T-cell prolymphocytic leukemia , ccl5, interaction analysis

Echinomycin and L-Asparaginase induce apoptosis in acute lymphoblastic leukemia cell line (Research Paper)

Mozhgan Zolfaghari,[1] Mahnoosh Abbaszade Dibavar,[2] Amir Atashi,[3,*] Reyhaneh Abriyan,[4]

1. Department of Biochemistry, Faculty of Sciences, Payame Noor University, Tehran, Iran
2. Department of Hematology and Blood Banking, School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Department of Medical Laboratory Sciences, School of Allied Medical Sciences, Shahroud University of Medical Sciences, Shahroud, Iran
4. Department of Medical Laboratory Sciences, School of Allied Medical Sciences, Shahroud University of Medical Sciences, Shahroud, Iran

Introduction: One of the best approaches for cancer therapy is combinational chemical drug therapy. Echinomycin and L-Asparaginase, have therapeutic effects on Acute Lymphoblastic Leukemia (ALL) with known side effects in various cases. Combination of these drugs maybe lead to reduced dose of each one and eventually decreased side effects. In this experimental study, the effects of combinational usage of these drugs was studied on a lymphocytic leukemia cell line.

Methods: Jurkat cells were cultured in RPMI 1640 culture medium containing 10% FBS and L-glutamine. MTT assay was performed to find IC50 concentration of L-Asparaginase, Echinomycin and combination of them. Annexin V-PI apoptosis assay was also done by flow cytometry to assess apoptotic effects of L-Asparaginase, Echinomycin and their combination.

Results: The synchronized effect of two drugs (Echinomycin and l-Asparaginase with a concentration of 0.025 µM and 0.012 IU/ml, respectively) was 25%. The rate of apoptosis in a single dose of Echinomycin at a concentration of 0.025 µM, is 25%.

Conclusion: That is, despite decreased dose of drugs, but the degradation of the cells has not diminished, indicating the synergistic effect of the two drugs.

Keywords: Echinomycin, L-Asparaginase, Acute Lymphoblastic Leukemia, Apoptosis

Effect and comparison the immunogenicity of different adjuvants in the experimental Neospora caninum vaccine in mice (Research Paper)

Seyedeh zahra Bootorabi,[1] Ahad Olyaei,[2] Mohammad mehdi Namavari,[3,*]

1. Department of Veterinary Medicine, Kazerun Branch, Azad University, Iran
2. Department of Veterinary Medicine, Kazerun Branch, Azad University, Iran
3. Shiraz Branch, Razi Vaccine and Serum Research Institute, Agricultural Research, Education and Extension Organization (AREEO), Shiraz, Iran

Introduction: Neospora caninum is an intracellular protozoan of the Apicomplexa and a cause of neosporosis, which has worldwide distribution, and is considered to be the most important cause of abortion in cattle causing many losses. So, It is an important economic issue around the world. Previously, various vaccine formulations have been measured and vaccines with live-attenuated strains have shown the most promising results in terms of protection. Adjuvants as auxiliary substances are important components of vaccines and using them is to improve the effectiveness of vaccines and increasing their immunity. Adjuvants enhance the cellular and humoral immune responses. In this research; we evaluated Neospora caninum live-attenuated strain with various adjuvants as the form of an experimental vaccine in BALB/C mice as the best laboratory model for neosporosis disease.

Methods: Sixty mice were randomly divided into ten equal groups, including the control, live-attenuated strain without adjuvant, live-attenuated strain with Aluminum hydroxide adjuvant, live-attenuated strain with Montanide oily adjuvant, live-attenuated strain with Chitosan adjuvant in four different groups with percentages of 25, 50, 70, 90% with Sigma brand, live-attenuated strain with Chitosan adjuvant with 90% percentage with Iranian brand and live-attenuated strain with combined adjuvant. They were all immunized in two phases with four weeks apart. Agglutination test and ELISA test were used to measure the humoral immunity response and gamma interferon test was used to measure cellular immunity response.

Results: The results showed that the group with live-attenuated strain with combined adjuvant produces the highest cellular and humoral immune response. The results also showed that mice immunized with live-attenuated strain with Iranian brand Chitosan adjuvant had a very good humoral and cellular response and were significantly different from the control group (Pv <0.05) and there is no significant difference in the immunized group with live-attenuated strain and with Sigma brand chitosan adjuvant.

Conclusion: In sum, the results of this study showed that; The research on Neospora caninum live-attenuated vaccine along with the combined adjuvant, is effective in mice to cause humoral and cellular immune response and immunization of mice with this is safe and completely effective method. Therefore, it is suggested that this experimental vaccine is used in additional research in order to achieve a functional vaccine for controlling the infection caused by Neospora caninum in farm animals such as cattle and sheep and even in dogs.

Keywords: Neospora caninum, adjuvants, immunization, mice, vaccine

Effect of Nickle chloride on element levels in the bone tissue of Wistar rats: calcium phosphor changes (Research Paper)

Zahra Azmoun,[1] Seyed Mohammad Hosseini,[2,*] Sohrab Kazemi,[3]

1. Department of Pathology, Islamic Azad University, Babol Branch, Babol, Iran
2. Department of Pathology, Islamic Azad University, Babol Branch, Babol, Iran
3. Cellular and Molecular biology research centre, health research institute, Babol University of medical sciences

Introduction: Nickel (Ni) and its compounds are frequently used in industrial and commercial products such as stainless steel, alloys, and batteries. since human activities are the major cause of pollution, and metals can enter the food chain and bioaccumulate in hard and soft tissues/organs, which results in a long half-life of the metal in the body. The present review focuses on (Nickel II chloride) and its effects on bone tissue. excess of this metal in the body can alter bone dynamics. Long-term exposure to high concentrations induces an imbalance in the bone mineral remodeling process. Different doses of Nickel are evaluated on element levels in the bone tissue in order to demonstrate these results.

Methods: 32 female Wistar rats were separated into 4 groups. The first group obtained water without treatment whilst three other groups received nickel by doses of 10, 15, and 25mg/kg, sequentially. All items were injected intraperitoneally and carried out thrice on days 8, 12, and 16. After 20 days, in order to evaluate biochemical values of calcium and phosphorus, blood samples were taken from every rat. Ultimately, rats were euthanized under general anesthesia by Ketamine and Xylazine.

Results: Although a dose-dependent increase in levels of calcium and phosphorus has been shown, the alterations between groups were not observable. Nevertheless, the calcium and phosphorus of the control group were at minimum levels. As nickel dose rises, calcium and phosphorus levels get higher. Thus, the highest levels belonged to nickel dose 25mg/kg treated rats.

Conclusion: Through this research, it can be manifested by elevated levels of calcium and phosphorus that nickel can cause destructive effects on rats, and kidney lesions should be considered as subsequences of nickel intakes.

Keywords: Nickel, Phosphor, calcium, bone tissue, Wistar Rat

Effect of Glucagon-like peptide-1 receptor agonists (GLP-1 RA) on serum uric acid concentration: A systematic review and meta-analysis (Review)

Milad Bahrami,[1,*] Sara Najafi,[2] Amirhossein Sahebkar,[3]

1. Student Research Committee, Faculty of Paramedical Sciences, Mashhad University of Medical Sciences, Mashhad, Iran
2. Student Research Committee, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
3. Applied Biomedical Research Center, Mashhad University of Medical Sciences, Mashhad, Iran; Biotechnology Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran; School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran.

Introduction: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are a class of medications used to treat type 2 diabetes. They improve glucose tolerance, increase insulin secretion, and induce weight loss. There is a controversy over the effect of GLP-1 RAs on serum uric acid (SUA) concentration. Our systematic review attempts to objectively answer whether GLP-1 agonists affect the serum levels of uric acid.

Methods: We performed a systematic search on Pubmed, Web of Science, Embase, Scopus and Google Scholar datasets up to 27 August 2021 with a language restriction of English only. Randomized controlled trials, observational studies, uncontrolled trials, and conference abstracts were included in, and studies with insufficient data, irrelevant types of study and follow-up duration of less than a month were excluded from the review. After critical appraisal by Joanna Briggs Institute checklists, articles underwent data extraction using a pre-specified Microsoft Excel sheet.

Results: Of 1004 identified studies, 20 were eligible for our systematic review. Pre- to post-administration analysis of GLP-1 RAs effects on SUA demonstrated that GLP-1 RA could significantly reduce SUA concentration (P-value<0.001). However, when compared to placebo, GLP-1 RAs did not significantly lower SUA concentration (P-value=0.122). Surprisingly, the active controls (including insulin, metformin, iGlar, SGLT-2 inhibitors, and DDP-4 inhibitors) could significantly alter SUA concentration more than GLP-1 RA (P-value<0.001).

Conclusion: The use of GLP-1 agonists can result in a significant reduction in the serum uric acid concentration. However, this reduction is not as much as that seen in insulin, metformin, iGlar, and SGLT-2 inhibitor users.

Keywords: Uric acid, Glucagon-like peptide-1 receptor agonists, GLP-1 RA, diabetes mellitus

Effect of high fat diet with corn oil on PGC-1α and UCP1 gene expression in adipose tissue of Sprague-Dawley rats (Research Paper)

Babak Hassankhan,[1,*] Parichehreh Yaghmaei,[2] Kazem Parivar,[3] Azadeh Ebrahim-Habibi,[4]

1. Department of Biology, Faculty of Basic Sciences, Science and Research Branch, Islamic Azad University, Tehran, Iran
2. Department of Biology, Faculty of Basic Sciences, Science and Research Branch, Islamic Azad University, Tehran, Iran.
3. Department of Biology, Faculty of Basic Sciences, Science and Research Branch, Islamic Azad University, Tehran, Iran
4. Endocrinology and Metabolism Research Center, Tehran University of Medical Sciences, Tehran, Iran.

Introduction: Background and Aim: Excessive dietary fat consumption and composition of fatty acids in diet plays an important role in health and body weight gain. Previous reports suggest that high omega-6 polyunsaturated fatty acids (PUFA) in diet may associate with metabolic syndrome and Non-alcoholic fatty liver disease (NAFLD). A higher amount of n-6 PUFA leads to increase pro-inflammatory cytokines, which contribute towards inflammation and insulin resistance. PGC-1α is a transcriptional coactivator and it plays an important role in the control of cellular energy metabolism. Reduced PGC-1α gene expression in adipose tissue have been associated with obesity and insulin resistance. Expression of PGC-1α was associated with UCP1 upregulation in some adipose tissue. Uncoupling protein 1 (UCP1) is a mitochondrial membran protein in brown adipose tissue (BAT) and it is a chief regulator of energy expenditure in this tissue. In the present study, a high-fat emulsion diet with corn oil (contains high values of omega-6 PUFA) was used to evaluate its effect on obesity, insulin resistance, PGC-1α and UCP1 gene expression in male Sprague-Dawley rats.

Methods: Materials and Methods: Sixteen male rats were divided into normal control group (n=8) and high fat group (n=8). The normal control group received a standard diet. The high fat group received a standard diet and received a high fat emulsion diet containing corn oil by gavage daily for six weeks. After this time, the rats were sacrificed. Blood samples were collected for measurement of biochemical parameters includ serum lipid profile, glucose, insulin, insulin resistance (HOMA-IR), liver enzymes, adiponectin (Adip) and tumor necrosis factor α (TNF-α). Liver tissue was homogenized for measurement of lipid profile and hepatic malondialdehyde (MDA). Liver histological tests with hematoxylin-eosin staining were performed to evaluate fat accumulation in liver tissue. Retroperitoneal adipose tissue was collected for measurement of PGC-1α and UCP1 gene expression by Real-time PCR.

Results: Results: After six weeks, the level of lipid profile, glucose, insulin, insulin resistance (HOMA-IR), TNF-α, in serum and hepatic content of malondialdehyde (MDA), and triglyceride (TG) significantly increased (P<0/05) and serum adiponectin significantly decreased in high fat group compared to the normal control group (P<0/05). Liver sections of high fat group displayed obvious fat droplets and macrovesicular steatosis. The level of PGC-1α and UCP1 gene expression decreased in high fat group compared to the normal control group.

Conclusion: Our results showed that high omega-6 PUFA in diet are associated with reduction of PGC-1α and UCP1 gene expression in retroperitoneal adipose tissue. Reduction of PGC-1α alter adipose tissue metabolism and mey predispose the person to a higher risk of NAFLD. Hence, PGC-1α may be considered as a target for treatment of NAFLD.

Keywords: Non-alcoholic fatty liver disease, PGC-1α, Omega-6 polyunsaturated fatty acids, Insulin resistance

Effect of liposomes containing nettle essential oil on Pseudomonas aeruginosa and Escherichia coli as nosocomial infections (Research Paper)

Mostafa rahimi nasab,[1,*] Ruholla rahimi nasab,[2] Mohammad Javad Forouzani-Moghaddam,[3]

1. Bachelor of Biotechnology, Yazd University, Yazd, Iran
2. Bachelor of Biotechnology, Yazd University, Yazd, Iran
3. Msc of Food Microbiology, School of Paramedical, Iran University of Medical Sciences, Tehran, Iran

Introduction: The aim of this study was to investigate the antibacterial effect of liposome containing nettle essential oil. For this purpose, the lipid system containing nettle essential oil has been synthesized for nosocomial infections Pseudomonas aeruginosa and Escherichia coli antibacterial methods.

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 tests were then performed to evaluate the performance of nanoparticles containing clove essential oil on Pseudomonas aeruginosa and Escherichia coli.

Results: The average particle diameter was 46 nm and its zeta potential was -13.8 mV. The loading rate in nanoparticles was 76%, which was calculated by reading the absorption of light from the standard Trachyspermum Copticum curve. The minimum inhibitory concentration (MIC) of Pseudomonas aeruginosa and E.coli for nanoparticles was 62.5 and 31.25 mg / ml.

Conclusion: Nanoparticles containing nettle essential oil kill nosocomial infections Pseudomonas aeruginosa and Escherichia coli and can be used as antibacterial nano-systems.

Keywords: Nettle, Antibacterial, Pseudomonas aeruginosa, Escherichia coli

Effect of nanocurcumin on skin cell lines (Research Paper)

Houshang Nemati,[1,*] Mohammad hosein Ghahremani,[2] Sayed Hamid Madani,[3] Alireza firoz,[4] Ghobad Mohammadi,[5] Mehri Nazeri,[6]

1. Fertility and Infertility Research Center, Health Technology Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran
2. Department of Pharmacology and Toxicology, Faculty of Pharmacy, Tehran University of Medical Sciences
3. Department of pathology, Faculty of medicine, Kermanshah University of Medical Sciences
4. Faculty of Medicine, Tehran University of Medical Sciences
5.
6. Fertility and Infertility Research Center, Health Technology Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran

Introduction: Psoriasis is a skin disease that causes red, itchy scaly patches, most commonly on the knees, elbows, trunk and scalp. Application and systemic delivery of small interfering RNAs offer many effective therapeutic advantages for gene regulation in the skin.

Methods: In this study, the final concentration of 50 μM nano-curcumin at the time point of 48 h was chosen. Then we monitored suppression of EGF, EGFR, VEGF, IL8 and IL17 genes after treatment of A431 cells by SNA-NCs. The expression of genes was validated by qRT–PCR in A431 cells.

Results: Results showed that the curcumin-nanoparticles were stable and non-toxic. Experiments showed that curcumin conjugated with spherical nucleic acid gold nanoparticles can significantly reduce EGF, EGFR, and VEGF gene expression in cells.

Conclusion: Curcumin is a natural substance that is known to have anti-carcinogenic and anti-inflammatory effects against several types of cancers. A disadvantage of free curcumin is that it is highly hydrophobic and is poorly absorbed after oral administration. It seems that, nano-curcumin has a direct anti-proliferative effect on A431 cell lines. We found that nano-curcumin significantly up-regulated the expression of the growth genes.

Keywords: Nanoparticles, Curcumin, Skin cells, EGF, EGFR,

Effect of Topical Areca Palm Nuts Hydroalcoholic Extract on Burn Wound Healing in Rats (Research Paper)

Seyyed Mojtaba Ghorani,[1,*]

1. Islamic Azad University, Tehran Medical Branch

Introduction: Wound healing is a complex and dynamic process that begins immediately after tissue injury and continues until the wound has healed and been remodeled. Applying the most effective methods of burn repair is an ongoing challenge in medicine. Recent investigations and animal studies demonstrate that Areca palm, a slender palm from the Arecaceae family, nuts have multiple therapeutic properties including anti-ulcerogenic and wound healing effects. The present study was planned to evaluate the possible burn wound healing effect of hydroalcoholic extract of Areca palm nuts in rats.

Methods: In this experimental study, 40 male Wistar albino rats were examined in five groups of eight receiving silver sulfadiazine cream 1% (reference standard), eucerin (positive control), 5% and 10% ointments of Areca palm nut hydroalcoholic extract (treatment groups) for 14 days. Negative control group received no treatment. Burn wounds were made on the dorsal part of the animals' necks. Wound contraction rate and histopathologic study of wound sites after sacrificing the rats were performed. Data were analyzed using SPSS software version 22.

Results: On the 14th day, wound contraction rate (WCR) was significantly higher in rats treated with Areca palm 10% extract ointment compared with 5% extract, positive and negative control groups ($P < 0.001$) and SSD ($P=0.01$). Application of 10% extract ointment on burn wound sites showed complete healing and slight tissue inflammation and edema.

Conclusion: These results suggest that the hydroalcoholic extract of Areca palm nuts could accelerate the wound healing process. Further study is required to identify the compounds responsible for its wound healing properties and to understand the mechanism of action.

Keywords: Areca catechu, Hydroalcoholic extract, Burn wound, Wound contraction, Wound healing.

Effect of Turmeric on Adiponectin, Sexual behavior and sexual Hormones in stressed Mice (Research Paper)

Elahe Sadeghi Sahebzad,[1] Najmeh Tehranian,[2,*] Anoshirvan Kazemnejad,[3] Mohsen Sharifi,[4] Faraz Mojab,[5]

1. Department of Reproductive Health and Midwifery, Faculty of Medical Sciences, Tarbiat Modares University
2. Department of Reproductive Health and Midwifery, Faculty of Medical Sciences, Tarbiat Modares University
3. Department of Biostatistics, Faculty of Medical Science, Tarbiat Modares University
4. Department of Plant Biology, Tarbiat Modares University
5.

Introduction: Sexual behavior is essential for species survival. Adiponectin is one of the hormones that modules the levels of dopamine, melanocortin, progesterone, and estrogen. So it can improve sexual function. Turmeric is an accessible plant and in various studies shows its ability to increase serum adiponectin levels. Therefore, the researcher decided to conduct a study to determine the effect of turmeric on serum adiponectin levels, sexual behavior, and profile of steroid hormones in stressed mice

Methods: 30 mice 6 in each group, were used in the current study. The mice first underwent blood sampling. Then all mice were subjected to stress testing before the intervention except one group, which considered as a control group. The intervention in this study was done as a 100 mg/kg turmeric extract that was gavaged daily for each mice. After the intervention, all mice were tested for sexual behavior, and then blood samples were taken to check serum levels of adiponectin, estradiol, progesterone and prolactin

Results: the results showed before the intervention there were no significant difference among 5 group in levels of adiponectin ($p=0.145$), estradiol ($p=0.148$), progesterone ($p=0.166$) and prolactin ($p=0.206$) but after intervention there were significant difference between 5 group in levels of adiponectin, estradiol and progesterone ($p<0.001$). Also there was significant difference among 5 groups in sexual behavior ($p<0.001$)

Conclusion: Therefore, consumption of turmeric, which increase serum adiponectin in the stressed mice, can improve sexual behavior and estradiol hormones Profiling.

Keywords: Mice, Sexual behavior, Hormones, Adiponectin

Effectiveness of Image-based module in clinical nursing education program in dermatology (Research Paper)

Elaheh Mojab,[1,*]

1. Nursing Department, Shiraz University of Medical Sciences

Introduction: Clinical education is a dynamic process, which students gradually gain experience by being present at the patient's bedside and applying the learned concepts in practice in interaction with the instructor, the environment, and the patient. Clinical education is affected by many challenges, including lack of time and facilities, as well as clinical cases. Identifying common skin lesions and providing appropriate care for dermatology patients is one of the purposes of learning skin diseases and nursing care in the dermatology course. Using technology and interactive methods can partially solve the challenges of clinical education. The present study aimed to investigate the effectiveness of using an image-based module of skin diseases and lesions in improving the knowledge of nursing students in dermatology.

Methods: This quasi-experimental study was performed on 74 nursing students. Sampling was done by census method and the participants were divided into two groups: control and experimental. The training program was first presented in the control group by using the common method in the dermatology nursing course and then in the experimental group by adding an image-based module with the common teaching method; then, using a researcher-made knowledge assessment questionnaire, students' knowledge in identifying and diagnosing skin lesions was assessed in both groups.

Results: Results showed that the image-based module of skin lesions has improved nursing students' knowledge about skin lesions. The mean score of students' knowledge in the experimental group (63.85%) was higher than the control group (46.41%).

Conclusion: Concerning the visual nature of skin lesions, the use of an image-based module can affect the knowledge of nursing students in the clinical education, examination, and diagnosis of skin diseases. It is suggested that image-based tools and modules can be used as an educational resource in clinical education to make it more effective.

Keywords: Nursing Education, Image-based learning, module, knowledge, dermatology

Effects of 8-hydroxyquinoline-coated graphene oxide on cell death and apoptosis in breast (MCF-7) and colorectal (SW742) cancer cell lines (Research Paper)

Firouzeh Kheiltash,[1,*] Kazem Parivar,[2] Nasim Hayati Rodbari,[3] Behnam Sadeghi,[4] Alireza Badiei,[5]

1. Department of Biology , North Tehran branch , Islamic Azad University , Tehran , Iran
2. Department of Biology , Science and Research branch , Islamic Azad University , Tehran , Iran
3. Department of Biology , Science and Research branch , Islamic Azad University , Tehran , Iran
4. Cancer Immunotherapy and Regenerative Medicine Breast Cancer Research Center , Motamed Cancer Institute , ACECR , Tehran , Iran
5. School of Chemistry , College of Science , University of Tehran , Tehran , Iran

Introduction: Introduction: Breast and colorectal cancers are of the major causes of cancer-related death worldwide. The anticancer properties of 8-hydroxyquinoline (8HQ), and the increasing use of graphene oxide (GO) as a drug delivery system with anti-cancerous properties, led us to investigate toxicity and apoptosis-induction capability of 8HQ-coated GO on breast and colorectal cancer cells compared to normal breast cells.

Methods: Methods: The breast cancer (MCF-7), colorectal cancer (SW-742) and normal breast (MCF-10) cell lines were treated with several doses of 8-HQ-coated GO for 12, 24, and 48 hours. The toxicity of nanocomposite was measured using MTT assay and the effect of nanocomposite on cell apoptosis were determined by examining the expression of P53, P21, Bax and Bcl-2 genes, as well as Annexin-V /PI apoptosis assay.

Results: Results: There were significantly increased cell death in nanocomposite-treated colorectal and breast cancer cells, especially MCF-7, compared to treated normal breast cells. A significant increased expression of P53, P21 and Bax genes and reduced expression of Bcl-2 gene were found in both treated cancer cell lines compared to the normal breast cell line. Annexin-V/PI assay also illustrated a significant induction of apoptosis in the cancerous cell lines, especially MCF-7, following nanocomposite treatment

Conclusion: Conclusion: Overall, 8HQ-coated GO has toxicity for breast and colorecctal cancer cell lines, and one of the mechanisms through which this nanocomposite can induce cell death is induction of apoptosis. With

complementary and in vivo studies, this nanocomposite can be suggested as a nano-drug with anti-cancer properties.

Keywords: Keywords: Graphene oxide, 8-Hydroxyquinoline, Breast Cancer, Colorectal Cancer, Apoptosis

Effects of Anti-RANKL and anti-Sclerostin monoclonal antibodies on estrogen deficiency-induced osteoporosis (Review)

Ava Resae,[1,*]

1. Researcher

Introduction: Osteoporosis is a metabolic bone disease caused by an imbalance in bone resorption and bone remodeling, and characterized by low bone mass and compromised trabecular architecture. Menopause, ovarian failure, ovariectomy and estrogen or testosterone deficiency can speed up skeletal catabolism and lead to osteoblast malfunction, increased osteoclastogenesis and osteoporosis. The treatment of estrogen deficiency-induced osteoporosis is still a challenge and most of the current therapeutics come with many side-effects. More therapeutic strategies are needed for the prevention of osteoporosis caused by estrogen deficiency, ovariectomy and menopause.

Methods: In this review article, the therapeutic effects of anti-RANKL and anti-Sclerostin antibodies were studied. Keywords such as “Osteoporosis”, “estrogen-deficiency”, “bone loss”, “monoclonal antibodies” and “ovariectomy” from 2018-2021 were searched in PubMed, Elsevier and google scholar, and review articles were excluded. One hundred and seventy-four articles were found. One hundred and twenty-nine of them were eliminated upon reading the title or abstract.

Results: Two major monoclonal antibodies made for the treatment of estrogen deficiency-induced bone loss are denosumab (anti-RANKL) and romosozumab (anti-Sclerostin). RANKL/RANK plays a significant role in osteoclastogenesis. RANK is expressed on osteoclast precursors and is activated by RANKL which leads to osteoclast maturation and bone resorption. Sclerostin is a secreted glycoprotein, mainly expressed by osteocytes that inhibits osteoblast differentiation and bone formation by inhibiting Wnt/β-catenin signaling pathway. Thus blocking the RANK/RANKL interaction or blocking sclerostin activity may be promising strategies for preventing osteoporosis. Studies on animals such as rodents, rabbits and monkeys showed a decreased number of active osteoclasts, increased bone mineral density and bone formation. Several short-term and long-term clinical trials on postmenopausal women or elderly men reported denosumab to be effective. It increased bone mineral density, decreased bone resorption and significantly decreased the risk of bone fracture. Many studies showed a combination of denosumab and teriparatide, or zoledronate to be equally effective. One study showed denosumab to be more effective than bisphosphate at improving bone mineral density, especially at lumbar spine, total hip and femoral neck. A recent study on ovariectomized rabbits showed

that using the combination of pulsed electromagnetic field (PEMF) technique along with the administration of sclerostin monoclonal antibodies leads to better results than single-drug therapy. One of the biggest disadvantages of denosumab and romosozumab is the reversibility of their therapeutic effects. In one study, romosozumab decreased bone resorption marker (β-CTX). However, its levels increased again upon discontinuation. Similar results have been noted in denosumab clinical trials. Many studies have reported that treatment effects of denosumab and romosozumab are reversible upon discontinuation, and patients who decide to discontinue them should rapidly transition to alternative treatments in order to prevent bone loss.

Conclusion: Overall, both anti-RANKL and anti-Sclerostin appear to enhance bone mineral density and have beneficial effects on both cortical and trabecular bone mass.

Keywords: osteoporosis, ovariectomy, menopause, monoclonal antibodies, denosumab

Effects of Arsenic on the macrophages in colorectal malignancy (Review)

Fatemeh Maghool,[1,*] Mohammad Hassan Emami,[2] Samane Mohammadzadeh,[3] Safoora Mohammadzadeh,[4]

1. Poursina Hakim Digestive Diseases Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
2. Poursina Hakim Digestive Diseases Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
3. Poursina Hakim Digestive Diseases Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
4. Poursina Hakim Digestive Diseases Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

Introduction: Cancer, as the most common leading cause of death, results from interactions between carcinogens and immune/non-immune cells. Macrophages are the professional phagocytes which help to recognizing the transformed cells and removing the immune-gene cancerous cells. Arsenic, as a chemical carcinogen, could result in the risk of cancer progression through induction of proliferation and apoptosis via activation of phosphatidylinositol 3-kinase (PI3K) /protein kinase B (AKT) signaling pathway. This review discusses role of arsenic on PI3K/AKT signaling pathway in the immune cells in colorectal cancer (CRC).

Methods: The English database were searched using the search terms "Arsenic", "macrophage", "PI3K/AKT signaling pathway", and "colorectal cancer" PI3K/AKT signaling pathway. Only published articles have been included.

Results: According to various studies, arsenic has powerful immune-toxic effects on immune cells, including macrophages. This heavy metal is capable to target the monocyte/macrophage by inhibiting differentiation, reducing endocytosis and phagocytosis activity, and inducing apoptosis. It could interfere with the antigen-presenting activity of macrophages. Arsenic induces immunosuppression that can lead to infectious diseases and cancers. Multiple molecular and cellular mechanisms can mediate arsenic immune-toxicity, including reactive oxygen species (ROS) production, alteration of redox-sensitive signaling pathways, DNA damage, epigenetic effects, and inflammasome inhibition. Multiple signaling pathways such as the PI3K/AKT pathway play a major role in immune-toxicity of As. PI3K/AKT pathway is one of the signaling pathways which regulates cell proliferation, cell cycle and apoptosis. Over-activation of this pathway may lead to malignant tumors and cancer progression. PI3Ks play role in phagosome formation, antigen-presenting and innate immune response. This pathway is normally activated

by extracellular signals including growth factors, cytokines and hormones and regulates macrophages activities. However, PI3K/AKT pathway could be inhibited directly or indirectly (through As-induced ROS) by arsenic toxicity, and ultimately promoted macrophage autophagy and dysfunctionalities. Therefore, As could alter macrophages activities (cytokine production, phagocytosis and antigen presentation) through inhibition of PI3K/AKT pathway.

Conclusion: in conclusion, arsenic has an immunosuppressive effect on macrophages by inhibiting the PI3K/AKT pathway which can help to progression of tumors in colorectal cancer.

Keywords: colorectal cancer, Arsenic, macrophage, PI3K/AKT signaling pathway

Effects of Boswellic Acid on the Cellular Toxicity and Proliferation of Glioblastoma Cell line (Research Paper)

Hamid Reza Moradi,[1] Zabihollah Khaksar ,[2] Sajad Sahabnegah ,[3] Ghadir Rajabzadeh ,[4] Sahar Salehi ,[5] Gholamhossein Tondro ,[6,*]

1. Department of Basic sciences, School of Veterinary Medicine, Shiraz University, Shiraz, Iran
2. Department of Basic sciences, School of Veterinary Medicine, Shiraz University, Shiraz, Iran.
3. Department of Neuroscience, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
4. Department of Food Nanotechnology, Research Institute of Food Science and Technology, Mashhad, Iran
5. Department of Food Nanotechnology, Research Institute of Food Science and Technology, Mashhad, Iran.
6. Department of pathobiology, School of Veterinary Medicine, Shiraz University, Shiraz, Iran

Introduction: Glioblastoma is one of the common subtype of primary brain tumors that has a higher mortality rate among the deadliest of human cancers. Boswellic acid (BSA) is a series of pentacyclic triterpene molecules that is isolated from the gum resin of Boswellia serrata. Medical properties of the BSA have previously been shown against various chronic diseases. This study investigated the effects of the BA on glioblastoma cell line (GCL) proliferation through MTT assay.

Methods: Glioblastoma cell line (1×104/well) were seeded in 96-well culture plates and kept at 37 °C in a humidified incubator (5% CO2) overnight. These cells were incubated with various concentration of BSA for the next 24, 48 and 72 h. After that, 10 µl of the MTT solution in PBS (5 mg/ml) was added to each well at a final concentration of 0.05%. After 4 h, the supernatant was removed and to dissolve the formazan crystals, 100 µl of dimethyl sulfoxide was added to each well. Then, the microplates were gently shaken in the dark for 60 min and the absorbance was assessed between 550 nm by a plate reader.

Results: Results showed that BSA significantly inhibited the proliferation of GCL in a concentration-time pattern. The IC50 value of BSA on GCL was 67µg/ml after 24 h, which decreased to 51µg/ml after 48 h and 48µg/ml after 72 h.

Conclusion: Summary, results of the current study shown that boswellic acid have the effect of cellular toxicity and inhibition of proliferation on glioblastoma cell line (U87) in a concentration-time pattern.

Keywords: Boswellic acid; Glioblastoma Cell Line (U87); MTT assay; Proliferation

Effects of dietary factors on the modification of breast cancer risk among high risk germline mutation/polymorphism carrier women (Review)

SayedAlireza Mousavi,[1] Fatemeh Karami,[2,*] Fatemeh Vaghefi,[3]

1. Department of Biology, School of Basic Science, Science and Research Branch, Islamic Azad University, Tehran, Islamic Republic of Iran
2. Department of Medical Genetics, Applied Biophotonics Research Center, Science and Research Branch, Islamic Azad University, Tehran, Islamic Republic of Iran
3. Department of Biology, School of Basic Science, Science and Research Branch, Islamic Azad University, Tehran, Islamic Republic of Iran

Introduction: Recently, effects of diet modifications have seized great attentions in decreasing the risk of cancer in high risk genetic alterations carriers. Owing to the extensive investigations on breast cancer, it was aimed to review the dietary factors which can alleviate or increase the risk of breast cancer among high risk mutation carriers.

Methods: We explored the internet in Google Scholar, Pubmed, Pubmed Central and Bing search engines using main key words including Breast cancer risk, gene polymorphism, gene expression, variant and dietary factors. All the manuscripts after 2000 were included in the present review.

Results: Eating red meat, coffee and alcohol were the most frequent dietary factors which have been assayed in hot spot mutation carriers. It was demonstrated that diets rich in red meat can dramatically increase the risk in BRCA1/2 mutation carriers. Coffee drinking could decrease the risk in BRCA1 carriers whereas the risk of breast cancer was different in heavy alcohol drinkers carrying hot spot variants.

Conclusion: Different dietary factors effects among mutation carriers is strongly indicating that personalized diet in addition to the mutation screening of high risk family members of breast cancer patients can remarkably reduce the burden of inherited breast cancer incidence. However, further studies are warranted to define the role of dietary factors on the overall risk of breast cancer among other gene variants carriers.

Keywords: Dietary factor, gene polymorphism, gene expression, breast cancer, risk

Effects of Elaeagnus angustifolia on induced oxidative stress by Arsenic in colorectal cancer (Review)

Aida Heidari,[1,*] Mohammad Hassan Emami,[2] Samane Mohammadzadeh,[3] Safoora Mohammadzadeh,[4]

1. 1-Poursina Hakim Digestive Diseases Research Center, Isfahan University of Medical Sciences, Isfahan, Iran , 2- Department of Cell and Molecular Biology and Microbiology, Faculty of Biological Sciences and Technologies, University of Isfahan, Isfahan, Iran
2. Poursina Hakim Digestive Diseases Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
3. Poursina Hakim Digestive Diseases Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
4. Poursina Hakim Digestive Diseases Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

Introduction: Colorectal cancer (CRC) is the third and fourth most leading cause of cancer mortality among men and women, respectively. Carcinogenic heavy metals, such as arsenic (As), are considered to be the major global public health problem and are correlated with various cancers, in particular colorectal cancer. Inorganic arsenic has been among the earliest cancer-causing agents in humans. Consequently, particular attention has been focused on plants with anti-cancer properties such as Oleaster (Elaeagnus angustifolia L.) to reduce the carcinogenicity of carcinogens. This review discusses the anti-carcinogenicity effects of Elaeagnus angustifolia L on As toxicity in CRC.

Methods: The electronic database were searched through the search words "Arsenic", "Elaeagnus angustifolia ", "oxidative stress", and "colorectal cancer". Only English articles have been included.

Results: As in the form of arsenite (As3+) or arsenate (As5+), triggers tissue damages and tumorigenesis in the CRC by generation of free radicals (reactive oxygen species, ROS), inflammation, lipid peroxidation, DNA damage, and activation of signaling pathways related to tumor promotion and progression. As- induced oxidative stress plays important roles in toxicity and carcinogenicity of arsenic, either directly or indirectly. Arsenic inhibits dehydrogenase and stimulates the activity of mitochondrial adenosine triphosphatase via the uncoupling of oxidative phosphorylation and therefore inhibits the formation of ATP during glycolysis. Furthermore, arsenic stimulates the production of pro-inflammatory cytokines tumor necrosis factor-α, interleukin 6 (IL-6), IL-8, and IL-12 in the plasma. Oleaster is a traditional herbal medicinal that has antioxidant, anti-inflammatory, antimicrobial, anticancer properties. The active components of Elaeagnus angustifolia are

flavonoids, phenolics, polysaccharides, amino acids, saponins, carotenoids, vitamins (tocopherol, carotene, vitamin C, thiamine B1), minerals (calcium, magnesium, potassium, iron and manganese), and tannins. Flavonoids and phenolic compounds exhibited antioxidant properties and antimicrobial activities through the release of electrons and scavenge the free radicals. Natural polyphenols, implicated in the defense against oxidative stress, and reduce the risk for many cancers. Polysaccharides have antioxidant activities that induce apoptosis and inhibit angiogenesis and metastasis through down regulation of matrix metalloproteinases and vascular endothelial growth factor. In addition, Tannins, terpenoids and lignanoid and bezenoid have anti-inflammatory, anti-cancer, and chemopreventive effects. Anticancer, anti-oxidative and anti-inflammatory properties of Oleaster may reduce As-induced oxidative stress and inflammation in colorectal malignancy.

Conclusion: Oleaster has anticarcinogenic effect on As toxicity in CRC because of its anti-oxidative and anti-inflammatory properties.

Keywords: Arsenic, Elaeagnus angustifolia , oxidative stress, colorectal cancer

Effects of Ginseng extract on immunopathological changes in experimental renal infection caused by Listeria monocytogeneses in mice (Research Paper)

Zahra Karamouz,[1] Seyed Zanyar Athari,[2] Younes Anzabi,[3] Daryoush Mohajeri,[4] Mir Alireza Nourazar,[5,*]

1. Faculty of Veterinary Medicine, Tabriz Branch, Islamic Azad University, Tabriz, Iran.
2. PhD Student at Medical Physiology, Faculty of Medicine, Tabriz University of Medical Science, Tabriz, Iran.
3. Department of Pathobiology, Faculty of Veterinary Medicine, Tabriz Branch, Islamic Azad University, Tabriz, Iran.
4. Department of Pathobiology, Faculty of Veterinary Medicine, Tabriz Branch, Islamic Azad University, Tabriz, Iran.
5. Department of Basic Sciences, Faculty of Veterinary Medicine, Tabriz Branch, Islamic Azad University, Tabriz, Iran.

Introduction: Renal infection with Listeria spp. usually happens after intraperitoneal exposure to the microorganism. Hydroalcoholic extract of Panax Ginseng has multiple immunomodulatory effects. Ampicillin is known as an effective antibiotic in the treatment of this disease. Therefore, this study aimed to evaluate the effect of hydroalcoholic extract of Ginseng compared to ampicillin on experimental renal infection caused by Listeria monocytogenes.

Methods: For this purpose 30 mice, 5-7 weeks, were randomly divided into five groups of 6 animals each including Healthy Control, Infected, Ampicillin treatment (20 mg/kg-sc), Ginseng Treatment (250mg/kg-sc), and Ginseng (250 mg/kg-sc)+Ampicillin (15mg/kg-sc) treatment groups. Blood samples were collected, and the concentration of serum creatinine, serum Urea, murine cytokines in serum, such as Interleukin-1 (IL-1), Interleukin-6 (IL-6), Interleukin-8 (IL-8), and Tumor necrosis factor- α (TNF-α) were measured by ELISA. Histopathological changes were evaluated in renal tissues. Data were analyzed by one-way ANOVA followed by Tukey test at the level of $p<0.05$ by SPSS and Graphpad software.

Results: Serum levels of IL-1, IL-6, IL-8, and TNF-α were significantly increased in the infected group ($p<0.05$). The cytokines significantly decreased in the Ampicillin+Ginseng treated group compared to the other experimental groups ($p<0.05$). Histopathological changes in kidney tissues were concomitant with biochemical findings.

Conclusion: The present study showed that the synergic effect of Ginseng extract and Ampicillin has an impressive efficacy on renal tissue injury caused by Listeriosis.

Keywords: Ginseng, Kidney, Listeriosis, Cytokines, Inflammation.

Effects of intrathecal and intracerebroventricular microinjection of kaempferol on pain: possible mechanisms of action (Research Paper)

sajjad jabbari,[1] maryam bananej,[2] Mohammad Zarei,[3,*] Alireza Komaki,[4] Ramin Hajikhani,[5]

1. Department of Biology, Faculty of Sciences, Islamic Azad University, Tehran North Branch, Tehran, I.R. Iran.
2. Department of Biology, Faculty of Sciences, Islamic Azad University, Tehran North Branch, Tehran, I.R. Iran
3. Neurophysiology Research Center, Hamadan University of Medical Sciences, Hamadan, Iran
4. Neurophysiology Research Center, Hamadan University of Medical Sciences, Hamadan, Iran
5. Department of Biology, Faculty of Sciences, Islamic Azad University, Tehran North Branch, Tehran, I.R. Iran

Introduction: Background and purpose: Kaempferol (KM), a flavonoid, has an anti-inflammatory and anticancer effect and prevents many metabolic diseases. Nonetheless, very few studies have been done on the antinociceptive effects of KM. This research aimed at assessing the involvement of opioids, gamma-aminobutyric acid (GABA) receptors, and inflammatory mediators in the antinociceptive effects of KM in male Wistar rats.

Methods: Experimental approach: The intracerebroventricular and/or intrathecal administration of the compounds was done for examining their central impacts on the thermal and chemical pain by the tail-flick and formalin paw tests. For assessing the role of opioid and GABA receptors in the possible antinociceptive effects of KM, several antagonists were used. Also, a rotarod test was carried out for assessing motor performance.

Results: Findings/Results: The intracerebroventricular and/or intrathecal microinjections of KM (40 g/rat) had partially antinociceptive effects in the tail-flick test in rats ($P < 0.05$). In the formalin paw model, the intrathecal microinjection of KM had antinociceptive effects in phase 1 (20 and 40 g/rat; $P < 0.05$ and $P < 0.01$, respectively) and phase 2 (20 and 40 g/rat; $P < 0.01$ and $P < 0.001$, respectively). Using naloxonazine and/or bicuculline approved the involvement of opioid and GABA receptors in the central antinociceptive effects of KM, respectively. Moreover, KM reduced the expression levels of caspase 6, interleukin-1β, tumor necrosis factor-α, and interleukin-6. The antinociceptive effects of KM were not linked to variations in the locomotor activity.

Conclusion: Conclusion and implications: It can be concluded that KM has remarkable antinociceptive effects at a spinal level, which is associated with the presence of the inflammatory state. These impacts were undetectable following injections in the lateral ventricle. The possible mechanisms of KM antinociception are possibly linked to various modulatory pathways, including opioid and GABA receptors

Keywords: Antinociception; Kaempferol; Pain; Spinal cord; Supraspinal.

Effects of Nickel chloride heavy metal on liver enzymes (ALT, AST, ALP) in Wistar Rats (Research Paper)

Ghazaleh sadeghnezhad,[1] Seyed Mohammad Hosseini,[2,*] Sohrab kazemi,[3]

1.
2. Department of Pathology, Islamic Azad University, Babol Branch, Babol, Iran
3. Cellular and Molecular biology research center, health research institute, Babol University of Medical Sciences, Babol, Iran

Introduction: Epidemiological investigations have demonstrated that numerous teratogenicity, carcinogenicity, respiratory diseases, and allergies of nickel compounds are not limited to occupational exposure but also the exposure of the population through foodstuff, drinking water, tobacco products Pipe tobacco, and cigarettes. The major target organs of nickel toxicity include the liver, kidney, brain, lung, and testis. This study aimed to evaluate the toxicity of nickel chloride on the activity of liver enzymes.

Methods: In this experimental study, 32 female Wistar rats weighing 200-210 g were housed in cages with eight rats per cage. The Control group, received a daily intraperitoneal injection (IP) of NaCl 0.9%. Nickel was given to the other three 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, blood samples were taken under deep anesthesia, serum separated by centrifugation was used for various biochemical estimations.

Results: Intraperitoneal administration of nickel chloride caused abnormal liver function in rats. In $NiCl_2$ 25mg/kg treated group the activities of serum liver marker enzymes such as serum aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase were significantly increased compared with the control group.

Conclusion: This study has shown that a high dose of NiCl2 administered by IP injection was able to induce hepatotoxicity. Furthermore, Serum results obviously indicate that the liver is susceptible to nickel induced toxicity

Keywords: Nickel, ALT, AST, ALP, liver, biochemistry, Wistar rat

Effects of Niosome Nanoparticle Containing Boswellic Acid on the Glioblastoma Cell Proliferation (Research Paper)

Hamid Reza Moradi,[1] Gholamhossein Tondro,[2] Soghra Gholami,[3] Sajad Sahabnegah,[4] Ghadir Rajabzadeh,[5] Zabihollah Khaksar,[6,*]

1. Department of Basic sciences, School of Veterinary Medicine, Shiraz University, Shiraz, Iran
2. Department of pathobiology, School of Veterinary Medicine, Shiraz University, Shiraz, Iran
3. Department of Basic sciences, School of Veterinary Medicine, Shiraz University, Shiraz, Iran
4. Department of Neuroscience, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
5. Department of Food Nanotechnology, Research Institute of Food Science and Technology, Mashhad, Iran
6. Department of Basic sciences, School of Veterinary Medicine, Shiraz University, Shiraz, Iran.

Introduction: The application of boswellic acid-loaded niosome nanoparticle (BA-NP) is a novel method that can promote the bioavailability and drug delivery activity of free boswellic acid. Human glioblastoma is the most prevalent primary brain tumors that has a higher mortality rate among human cancers. The purpose of this study was the effects of the BA-NP on glioblastoma cell line (GCL) proliferation through MTT assay.

Methods: Glioblastoma cell line (1×104/well) were cultured in 96-well plates and incubated at 37 °C in an atmosphere of 5% CO2 overnight. These cells were incubated with various concentration of BA-NP for the next 24, 48 and 72 h. Then, 10 µl of the MTT solution in PBS (5 mg/ml) was added to each well at a final concentration of 0.05%. After 4 h, the supernatant was removed and to dissolve the formazan crystals, 100 µl of dimethyl sulfoxide was added to each well. Then, the microplates kept in the dark (60 min) and absorbance was measured by an ELISA microplate reader at 550 nm.

Results: Our results showed that BA-NP significantly inhibited the proliferation of glioblastoma cell line in a time- and dose-dependent manner. The IC50 value of BA-NP on GSCs was 0.12 µg/ml after 24 h, which decreased to 0.037µg/ml after 48 h.

Conclusion: In conclusion, results of the current study shown that boswellic acid-loaded niosome nanoparticle have the effects of cytotoxicity and inhibition of proliferation on glioblastoma cell line (U87) in a time- and dose-dependent manner.

Keywords: Niosome Nanoparticle, Boswellic acid; Glioblastoma Cell Line (U87); MTT assay; Cytotoxicity

Effects of plant-derived polyphenols on the coronavirus treatment and prevention: a review (Review)

Mehdi Dehghani Kazemi,[1,*]

1. Department of Biology, Faculty of Science, University of Zabol, Zabol, Iran

Introduction: Polyphenols are non-flavonoids or flavonoids plant-derived metabolites with wide verities of biological properties including antioxidant, anti-inflammatory, anticancer, antidiabetic, prebiotic, hepatoprotective, neuroprotective and antiviral. This study aims at reviewing the literature concerning to the antiviral potentials of polyphenols in prevention or treatment of COVID-19 infection.

Methods: An extensive literature search was conducted from the onset of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) or the 2019 novel coronavirus at the end of 2019, using various databases including Google Scholar, and Scopus. Using different combinations of several keywords including COVID-19, infection, prevention and polyphenols. A total of 16 papers were selected for conducting this review.

Results: Like other coronaviruses, SARS-CoV-2, which is the seventh coronavirus infecting humans, is a 150–160 nm virus with positive single-stranded RNA, nucleoprotein, capsid, matrix, and S-protein, but unlike other coronaviruses it possesses an extra glycoprotein with acetylesterase and hemagglutination properties. The virus induces a spectrum of manifestations and affects respiratory, gastrointestinal, hematological, nervous, renal, and the immune systems, affecting more than 219 million people with 4.55 million deaths by September tenth 2021. There are several vaccines developed against the virus, while none of them provide complete protection due to consecutive mutations in its genetic material. Currently, only supportive care and non-specific treatment is available for this lethal disease. For these reasons, a complementary treatment or preventive strategy via biologically active natural products is highly necessary. The main protease of SARS CoV-2 is the key enzyme for the virus replication and transcription, thus serves as an important drug target for inhibiting the virus growth inside the hose. A comparison between six polyphenols of Broussonetia papyrifera with two anti HIV drugs (lopinavir and darunavir) against SARS CoV-2 main protease, showed that natural polyphenols are superior in inhibition of protease catalytic activity and halt of the virus replication, suggesting them as promising anti-COVID-19 drugs. Currently, various natural polyphenols from medicinal plants are extensively employed alone or as an adjunct to antiviral drugs against the virus worldwide. However, there are evidences that medicinal plants rich in resveratrol, quercetin, and kaempferol show a high efficacy against SARS-CoV-2, via interfering with the virus replication, inflammation, chemokine

production, vascular permeability, and virus-induced apoptosis. These three polyphenols show anti-oxidant, anti-inflammatory and autophagy induction effects synergistically and counteract the virus replication. The phenolic compounds sinigrin and hesperetin extracted from Isatis indigotica root, have also showed anti-SARS-CoV main protease activity. This prohibition has been attributed to floronates, flavonoids, and pseudo-peptides. There are other phenolic compounds counteracting SARS-CoV-2 through interacting with the receptor binding site and catalytic dyad of the main protease including pedunculagin, tercatain, castalin phacelianin, gentiodelphin, cyanodelphin, and tecophilin. The strongest SARS-CoV-2 inhibitors are among florotannin group (8,8′ -Bieckol, 6,6′ -Bieckol, Dieckol) and oligomers of phloroglucin (1,3, 5- trihydroxybenzene) extracted from the algae Ecklonia cava and Sargassum spinuligerum, respectively (Phaeophyceae). A study recommended daily consumption of Rubus idaeus, Rubus fruticosus, Punica granatum and specially Camellia sinensis (black tea) in early stages of the virus infection due to their high content of effective polyphenols against SARS-CoV-2 including Sanguiin H-6, Theaflavin 3,3'-Odigallate, Theaflavin 3-O-gallate, Kaempferol 3-Oglucuronide, Protocatechuic acid 4-Oglucoside, and Punicalagin.

Conclusion: The natural plant derived polyphenols represent a valuable potential for combating the multisystem COVID-19 pathogenesis due to their multi-system, multi-target, anti-inflammatory, antioxidant, antiviral, and immune promotor impacts along with low toxicity at recommended doses. Therefore, the potential Antiviral polyphenolic-based drugs will hopefully constrain the SARS-CoV-2 infection and duplication by mitigating the virus enzymes.

Keywords: polyphenols, COVID-19, drugs, prevention

Effects of Pomegranate fruit and Pomegranate molasses on induced oxidative stress by chromium in colorectal cancer (Review)

Samna Mohammadzadeh,[1,*] Mohammad Hassan Emami,[2] Safoora Mohammadzadeh,[3] Fatemeh Maghool,[4] Aida Heidari2,[5]

1. Poursina Hakim Digestive Diseases Research Center, Isfahan University of medical sciences, Isfahan, Iran
2. Poursina Hakim Digestive Diseases Research Center, Isfahan University of medical sciences, Isfahan, Iran
3. Poursina Hakim Digestive Diseases Research Center, Isfahan University of medical sciences, Isfahan, Iran
4. Poursina Hakim Digestive Diseases Research Center, Isfahan University of medical sciences, Isfahan, Iran
5. Department of Cell and Molecular Biology and Microbiology, Faculty of Biological Sciences and Technologies, University of Isfahan, Isfahan, Iran

Introduction: High levels of heavy metals such as chromium (Cr) in the environment are related with the colorectal cancer incidence. Cr induces toxicity and carcinogenesis via oxidative stress and oxidative tissue injuries. Cr-induced oxidative stress may promote colorectal cancer. Pomegranate and pomegranate molasses are the good sources of antioxidants, may be modulated Cr-induced damages. This review aims to highlight the protective properties of

Methods: For this review, the electronic database was searched using the search words colorectal cancer, Chromium, carcinogenesis, oxidative stress and pomegranate and pomegranate molasses. Only English published articles between 2000 until 2021 have been included.

Results: Chromium leads to oxidative stress by production of free radicals such as superoxide, singlet oxygen, nitric oxide, hydrogen peroxide, and the peroxylradical. This heavy metal could induce physiological and biochemical impairments by interacting with enzymes (eg., antioxidant enzymes), lipids, proteins, and genetic material (DNA and/or RNA). In addition, Cr- induced oxidative stress products could cause damages of membrane, degradation and deactivation of genetic material, and proteins (enzymes) directly or indirectly which led to antioxidant/oxidant imbalances, growth inhibition and programmed cell death activation. Pomegranate fruits (Punica granatum L.) and their molasses are natural agents which used in many in vitro and in vivo studies. Several studies reported that pomegranate had the highest anti-oxidative, anti-proliferative and pro-apoptotic effects on colorectal cell lines (HT-29, HCT116, SW480, SW620) and could reduce colon cancer risk. Pomegranate showed reduction of inflammation in HT-29 cancer cells by down-regulation of inflammatory signaling pathways, such as inhibition of

tumor necrosis factor-α, and cyclooxygenase2; and suppression of nuclear factor kappa B and Protein kinase B activities. In Caco-2 and HT29 colon cancer cells, pomegranate released mitochondrial cytochrome c into the cytosol, activated caspase-3 and -9, and down-regulated anti-apoptotic Bcl-xL, decreased cyclins expression, arrested cells in S phase of cell-cycle that resulted in induction of apoptosis and inhibition of proliferation. In vivo studies on mouse models showed that pomegranate could protect proteins and DNA against oxidation. Pomegranate and their molasses are a source of polyphenolic (such as anthocyanins and phenolic acids, anthocyanins, ellagitannins, and hydrolysable tannins), flavonoids, polysaccharides, vitamins, and minerals which could represent protective activity against oxidative stress by scavenging free radicals, and inhibiting oxidation of macromolecules. Moreover, some previous in vivo studies showed that pomegranate molasses had strong antioxidant properties, four times more than Pomegranate juice that could decrease lipid peroxidation, and increase superoxide dismutase activity. Antioxidant properties of pomegranate molasses is related to high levels of phenolic acid, flavonoid, vitamin C, gallic acid, rutin & ellagic acid. In an animal study, pomegranate molasses reduced both the toxicity and oxidative stress of toxic material. Anticancer, anti-oxidative and anti-inflammatory properties of pomegranate in particular pomegranate molasses probably could be reduced Cr-induced oxidative stress and inflammation in cancer sites and might accelerate the elimination of colorectal tumor.

Conclusion: Pomegranate and pomegranate molasses with powerful antioxidant, anti-inflammatory, anti-proliferative, and anti-tumorigenic properties assumed as promising chemopreventive agent which probably could decrease Cr- induced toxicity and could be used in combination with conventional treatments for cancer prevention.

Keywords: colorectal cancer, Chromium, carcinogenesis, oxidative stress, pomegranate, pomegranate molasses

Elderly and burn injuries: a ten-year analysis of 612 patients (Research Paper)

Zahra Haghani Dogahe,[1] Mohammadreza Mobayen,[2,*]

1. Burn and Reconstructive Medicine Research Center, Guilan University of Medical Sciences, Guilan, Iran
2. Burn and Reconstructive Medicine Research Center, Guilan University of Medical Sciences, Guilan, Iran

Introduction: With all the progress made in geriatric medicine, we expected to have a growing population of elderly soon. With burn injuries, as one of the most common unpredictable injuries to the elderly, it is essential to clarify the epidemiological pattern and factors related to worse outcomes in geriatric burn patients. We aimed to investigate burn characteristics in the elderly in Guilan province, IRAN, in ten years.

Methods: In this study, we conducted a retrospective analysis of burn patients aging 60yrs and over in Velayat Burn Center between 2010 and 2020. The data collected from the hospital information system included age, sex, marital state, occupation, residency, season and month of the incident, place of incident, total body surface area (TBSA), burn degree, cause of the burn, anatomical site of the injury, pre-injury morbidities, surgical managements, length of hospital stay and mortality.

Results: Among 612 patients, the mean age was 72.20±8.94 years. The female to male ratio was 1.14:1 with a total of 53.3% female burn patients. 94.90% of patients lived with family members. 59.3% lived in urban areas. Most of the burn injuries happened during winter and summer. 82.5% happened indoors. The mean total body surface area (TBSA) was 19.70±22.13%. The most common causes were flames (50%) and scald (44.3%). The total length of hospital stay (LOS) was 6.14±6.27 days. The overall mortality rate was 15%. About 73.4% of our patients had a history of an age-related pre-injury medical condition, mostly cardiovascular diseases. In expired patients, the most common burn agent was flames (83.7%), and the mean TBSA was 55.48±28.79%. Factors related to longer hospital stay were age (p-value=0.001), TBSA (p=0.000), and length of hospital stay (p=0.000).

Conclusion: We concluded that most of the burn injuries among the geriatric population happen indoors, during the first hours of the day, and on the first day of the week, making it essential to establish special prevention programs suiting these situations. On the other hand, with the increased life expectancy and the unpredictable nature of burn injuries, it is essential to identify risk

factors and establish prevention programs for the elderly. With lowering the movement of rural inhabitants to urban areas, improving the safety of apartments and nursing homes, educating nurses and parents about the dangers of children spending time alone with their grandparents, and warning the health care system about the threats for diabetic patients and patients with heart conditions it would be possible to lower the incidence and overall mortality of burn injuries in the elderly.

Keywords: Burn injuries, burn, geriatric, elderly, epidemiology, outcome.

emergence of SARS-CoV-2 variants; public health concerns and risks (Review)

Sobhan Sadeghiyan,[1,*] Seyed Reza Mohebbi,[2] Seyed Masoud Hosseini,[3] Shabnam Kazemian,[4] Mahsa Saeedi Niasar,[5] Hamid Asadzadeh Aghdaea,[6]

1. Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Research Center for Gastroenterology and Liver Diseases, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
4. Research Center for Gastroenterology and Liver Diseases, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
5. Research Center for Gastroenterology and Liver Diseases, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
6.

Introduction: The first case of a new coronavirus that cause severe acute respiratory syndrome was observed in December 2019 in Wuhan, China. From December 2019 until 24 September 2021, there have been more than 230 million confirmed cases of COVID-19, including approximately 4,700,000 deaths. The first submitted sequence of SARS-CoV-2 was collected from a Wuhan market worker on 26 December 2019. In first days of 2020, the sequence's accession number in the GenBank has been published (NC 045512). Due to the Covid-19 pandemic, several studies about sars-cov-2 mutations and phylogenetic analyses have been performed. WHO watch carefully variants and classify them to variant of interest (VOI), variant of concern (VOC), and Variant of High Consequence (VOHC). VOI is a variant with distinct genetic mutations that have been linked to receptor binding affinity alteration, decrease in antibody efficacy, and neutralization property through past infection or immune induction by vaccination, probable diagnostic failure, or escalation in pathogenesis, disease severity, or transmissibility. It can be classified as VOC if there is evidence of a boost in disease severity, transmissibility, neutralizing antibodies inefficacy, in vaccinated or previously infected individuals, or detection inability of diagnostic assays. If there are clear clinical and research evidence on decrease in effectiveness of prevention measures or medical countermeasures in comparison to past variants in society, it can be considered VOHC.

Methods: The Elsevier databases were used to conduct a targeted literature search. We searched for “coronavirus” and each of the following terms or phrases separately and in combination: “SARS-CoV-2,” “mutation,” “genome,” “variant,” and “genomic changes.”

Results: Previous studies revealed more than 5000 various variants comprised variants with synonymous mutations, non-coding regions mutations, frame-shift deletions, in-frame insertions, non-coding insertions, stop-gained variants, in-frame deletions, non-coding deletions, and missense mutations. D614G, L84S, G392D, L3606F, D448 deletion are significant changes in the virus genome. Up to now, the variants of concern by WHO included: Alpha(GRY clade), Beta(GH clade), Gamma(GR clade), Delta(G clade). Recently, the Delta variant (B.1.617.2) was found in India and after a while became the predominant variant globally. T19R, E156G, del157/158, L452R, T478K, D614G, P681R, P681R, and D950N mutations are the characteristic mutations of the delta variant.

Conclusion: Research findings revealed that Delta variant has significantly higher transmissibility properties and also studies showed that vaccine-induced immune response has a lower efficacy with regard to Delta. In addition, two variants of interest, Lambda (Gr clade) and Mu (GH clade) were found in Peru and Colombia, respectively that should be monitored more carefully.

Keywords: SARS-CoV-2, COVID-19, mutation, Variant, genomic changes

Enhanced Antibacterial Effects of Chitosan/polyethylene oxide nanofibrous hydrogels loaded with Henna and Thyme extract: Potential Applications as Wound Dressing (Research Paper)

Mahboubeh Kabiri,[1,*] Zahra Kharat,[2]

1. Department of Biotechnology (straight Ph.D), College of Science, University of Tehran
2. Department of Biotechnology (straight Ph.D), College of Science, University of Tehran;

Introduction: Wound healing is known as a complex pathophysiological process, necessitating deep caring strategies while preventing infection. Most cases of wounding often suffer from a high risk of bacterial and fungal infection, due to the disruption of the skin structure as the outermost defense barrier of the body. As such as appropriate wound dress would be necessary to prevent or diminish infection risk, as well as acceleration of wound healing. In Chinese and ancient medicine, plenty of herbal plants have been introduced having profound wound healing effects. Inclusion of such herbal extracts in wound dresses can show dual role in augmenting wound healing and preventing infection

Methods: In the present study we added Henna and Thyme extracts into nanofibrous hydrogels made from chitosan and polyethylene oxide. Two-nozzle electrospinning was invoked to fabricate composite nanofibers containing alcohol extract of Henna and Thyme. The weight ratio of polymers along with the concentration of herbal extracts were optimized. After achieving a uniform nanafiber sheet, the antibacterial activity of the control polymers (CS/PEO), the extracts and extract loaded dressings were assessed against both gram negative and gram positive bacteria. The dressings were morphologically characterized using SEM. Also hemo-compatibility and cyto-compatibility tests were done to affirm the suitability of the nanofibrous hydrogels in contact with blood and human tissues.

Results: We observed that the appropriate ratio of CS/PEO and the most suitable extract concentrations was obtained to be 7/3 (v/v) and 1% (v/v), respectively. Herbal extract loaded nanofibers exhibited a good inhibition zone against E. Coli and S. Aureous. The hemolysis test showed that the coatings had no adverse effect on red blood cells. Cytocompatibility assay indicated that the prepared nanofibrous hydrogel was absolutely biocompatible as tested with fibroblast cells.

Conclusion: Overall, the results of our study showed that our Henna and Thyme extracts loaded CS/PEO nanofibrous dressings can safely be used in

various medical fields such as wound dressing and implantation coating to prevent bacterial adhesion, growth and generally, infection.

Keywords: Wound healing, Wound dressing, Nanofibrous Hydrogel, Herbal Extract, Antibacterial Effect

Enhanced Frequency of CD19+IL-10+B Cells in Human Gastric Mucosa Infected by Helicobacter pylori (Research Paper)

Mahboobeh Nahid-Samiei,[1] Ghorbanali Rahimian,[2] Mohammadhadi Shafigh,[3] Fatemeh Taheri,[4] Mohammad-javadSanaei,[5] Nader Bagheri,[6,*]

1. Cellular and Molecular Research Center, Basic Health Sciences Institute, Shahrekord University of Medical Sciences, Shahrekord, Iran
2. Department of Internal Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran
3. Department of Internal Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran
4. Department of Pathology, Shahrekord University of Medical Sciences, Shahrekord, Iran
5.
6.

Introduction: CD19+IL-10+B cells are considered as a particular subset of immunosuppressive cells by producing interleukin 10 (IL-10), which plays an important role in infectious and autoimmune diseases. The aim of this study was to determine the number of CD19+IL-10+B cells in Helicobacter pylori (H. pylori) positive patients in comparison with H. pylori negative patients, and to determine the association with different clinical outcomes, such as gastritis and peptic ulcer disease (PUD), in infected patients.

Methods: We studied 25 infected patients with gastritis, 25 infected patients with PUD, and 25 patients negative for H. pylori. The number of CD19+IL-10+B cells was determined by immunofluorescence.

Results: The number of CD19+IL-10+B cells in patients infected with H. pylori was significantly 2.5-fold higher than uninfected patients ($P < 0.0001$). Also, the number of CD19+IL-10+B cells in infected patients with gastritis was significantly 1.45-fold elevated compared to infected patients with PUD ($P = 0.001$).

Conclusion: These results demonstrate that the increased number of CD19+IL-10+B cells in infected patients and its association with other cells may play an important role in the pathogenesis of H. pylori infection

Keywords: Helicobacter pylori; Gastritis; Peptic ulcer disease, Regulatory B cells

Enhanced osteogenic differentiation of human bone marrow-derived mesenchymal stem cell on polycaprolactone/ brushite nanofibrous scaffold (Research Paper)

Seyedeh Sara Shafiei,[1,*] yeganeh Nikakhtar,[2] Mehrnoush Fathi-roudsari,[3]

1. National institute of genetic engineering and biotechnology
2. National institute of genetic engineering and biotechnology
3. National institute of genetic engineering and biotechnology

Introduction: Bone tissue engineering (BTE) aims to develop effective methods for repairing or replacing damaged bone tissue based on using three factors including biological molecules, cells, and biocompatible scaffolds, simultaneously.

Methods: In this study, composite scaffolds consisting of dicalcium phosphate dihydrate (DCPD, brushite) as a bone phase mineral precursor with different weight percentages (0%, 1%, 3%, 5%, and 10%) in combination with polycaprolactone (PCL) were fabricated by electrospinning technique. To assess the properties of the fabricated electrospun scaffolds, different techniques were employed. The morphology and mechanical behavior of scaffolds were characterized using scanning electron microscopy (SEM) and tensile strength test, respectively. The bioactivity of scaffolds was assessed in simulated body fluid (SBF). 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 and, gene expression analysis by real-time PCR.

Results: The results showed that PCL/DCPD (3 Wt %) had the highest tensile strength (15.35 MPa) which indicates a significant increase compared to the pure PCL. Furthermore, hMSC seeded on scaffolds showed over 80% viability after 1, 3, 7 days of incubation. Also, the results showed that the addition of DCPD to the PCL significantly increased the alkaline phosphatase activity. The osteocalcin (OCN) gene expression in the composite scaffold showed a 6.1-fold increase compared to the pure PCL.

Conclusion: It is concluded that electrospun PCL/DCPD scaffolds with optimum concentration can be a proper candidate for bone tissue engineering applications.

Keywords: Brushite, Electrospun,osteogenic ,

Epigenetic roles of PIWI proteins and piRNAs in colorectal cancer (Review)

Fatemeh Sadoughi,[1,*] Seyyed Mehdi Mirhashemi,[2] Zatollah Asemi,[3]

1. Research Center for Biochemistry and Nutrition in Metabolic Diseases, Kashan University of Medical Sciences, Kashan, I.R. Iran
2. Metabolic Diseases Research Center, Research Institute for Prevention of Non-Communicable Diseases, Qazvin University of Medical Sciences, Qazvin, Iran
3. Research Center for Biochemistry and Nutrition in Metabolic Diseases, Kashan University of Medical Sciences, Kashan, I.R. Iran

Introduction: For years, it was believed that 98% of DNA was “junk” because of the non-coding parts; today, lines of researches have proven that these parts of DNA have some essential functions, as well. According to evidence, more than 70% of our genome is actively transcribed but protein-coding genes contain about 1–2% of the genome, and the major group of transcripts is noncoding RNAs (ncRNAs). NcRNAs are categorized by their function regulatory ncRNAs are one of the subclasses of them. Regulatory ncRNAs are also divided into two subtypes: small non-coding and long non-coding RNAs. P-Element induced wimpy testis (PIWI)—interacting RNA (piRNA) is one of the members of small non-coding group of RNAs and takes part in silencing transposons, epigenetic regulation, and reorganization of the genome. Some of these properties can provide an idea that piRNAs are associated with some cancer hallmarks containing cellular proliferation, apoptosis, metastasis, and invasion. Colorectal cancer (CRC) is a major cause of morbidity and mortality in both men and women around the world. This cancer is listed as the third common cancer after lung and breast cancer; Thus, finding novel methods for treating this cancer can be a help to many people around the globe.

Methods: We have tried to collect the evidence available on the application of PIWI proteins and their related RNAs in colorectal cancer. We have used diverse search engines for this purpose including Pubmed, Google Scholar, and Scopus.

Results: Dysregulation of some piRNAs can be observed in CRC cells; for instance, up-regulated PiR-54265 is related to the activation of STAT3 signaling pathway, up-regulated PiR-823 is associated with the expression of HSP family, and down-regulated PiR-1245 is associated with metastatic stages of colorectal cancer. Furthermore, the levels of PIWI proteins are also observed to be altered in CRC cells. The up-regulation of HIWI, PIWIL2, and PIWIL1 is confirmed by some research in CRC.

Conclusion: Accumulative evidence expresses that PIWI proteins and their related RNAs (piRNAs) can be used only for diagnostic or prognostic purposes in CRC and till now, no therapeutic effects are discovered for these RNAs. However, further investigations might enhance our knowledge on whether they can be used for therapeutic purposes or not.

Keywords: cancer, colorectal. PIWI, piRNA, diagnosis

Ethanolic extract of Hyssopus officinalis moderates blood parametric (glucose, total cholesterol and triglycerides) in alloxan-induced diabetic rats (Review)

Masumeh Salem,[1,*]

1. Student research Center, Baharestan 1 Education Office, Baharestan 1, Tehran, Iran

Introduction: Background and aim: Diabetes mellitus results from the autoimmune destruction of the insulin-producing beta cells in the pancreas. Subsequent lack of insulin leads to increased blood and urine glucose. Hyssopus officinalis is a medicinal plant which had been has various used in traditional medicine. Traditionally, this medicinal plant used for treatment of asthma, fever, epilepsy and has have anti-depressant effect. In addition, recent studied revealed that this plant has antioxidant effect. In the current study, the effect of ethanolic extract of Hyssopus officinalis on the levels of blood glucose, total cholesterol and triglycerides in normal and alloxan-induced diabetic rats were evaluated.

Methods: Materials and methods: The effect of intra-peritoneal administration of ethanolic extract of Hyssopus officinalis (5, 10 and 20 mg/kg) for 15 days consequently on the level of serum glucose, total cholesterol and triglycerides in normal and alloxon-induced diabetic rats were evaluated.

Results: Results: Intra-peritoneal administrations of Hyssopus officinalis extract significantly decreased blood glucose, total cholesterol and triglycerides in diabetic rats but not in normal rats. The administration of Hyssopus officinalis extract did not change the serum parameters in normal rats. A comparison was made between the action of Hyssopus officinalis extract and glibenclamide (20 mg/kg), the known antidiabetic drug. The antidiabetic effect of the extract was the same of that observed with glibenclamide.

Conclusion: These finding revealed that this plant has hypoglycemic and hypolipidemic activities. It is concluded that this plant can be considered as excellent candidate for future studies on diabetes mellitus.

Keywords: Hyssopus officinalis, diabetes, glucose, total cholesterol, triglycerides

Evaluate the immune system of menopausal women with vasomotor symptoms against coronavirus and provide solutions to strengthen it (Review)

Seyed Mohammad Hossein Sabzpoushan,[1,*] Dr. Vahid Azizi,[2] Mahsa Ghiasvand,[3] Seyedeh Mahtab Mosanen Tabatabaei,[4] Fereshte Norouzdamghani,[5]

1. Department of Animal Sciences and Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran,Iran
2. Department of Animal Sciences and Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran,Iran
3. Department of Animal Sciences and Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran,Iran
4. Department of Animal Sciences and Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran,Iran
5. Department of Animal Sciences and Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran,Iran

Introduction: The purpose of this article is to investigate the risk of Covid-19 in postmenopausal women with symptoms of hot flashes (one of the symptoms of vasomotor), as well as to provide methods other than the use of chemical drugs to strengthen the immune system and fight the coronavirus in These are people.

Methods: Menopausal women experience many changes due to decreased levels of sex hormones, such as changes in the body's metabolism, cognitive behaviors, and so on. One of the most important and common changes is the onset of vasomotor symptoms. In such cases, depending on the individual's lifestyle and history of the disease, the autonomic nervous system will not be able to control the body's internal environment and induce an appropriate response. The most important clinical sign that appears in this condition is hot flashes. Rising body temperature, profuse sweating, is some of the complications that occur in women during hot flashes. At this time, the person suffers from a very high level of cognition stress and in the face of external stimuli, Fight-or-flight behaviors due to elevated levels of hormones such as cortisol and adrenaline appear in him. If this continues, the immune system will be weakened. Both innate and adaptive immune systems (1,2) interact to protect against pathogens. In Covid-19 disease, the virus enters the body and releases inflammatory cytokines such as interleukin-β-1, IL-6, IL-8, IL-2 into the bloodstream. These cytokines and chemokines call immune cells, especially monocytes and T lymphocytes, to the site of infection during the phenomenon of chemotaxis , which, along with cell swelling, reduces the efficiency of gas exchange in the lungs(3) .Infection is first activated by innate immunity and then by acquired immunity. In viral infections such as corona,

where the virus attacks target cells, cellular immunity has a more effective defense against the virus, which depends on the activation of B and T lymphocytes (4). The killer 〖CD8〗^+ T cells are responsible for identifying and then attacking directly infected virus cells. 〖CD4〗^+ cells are essential for stimulating lethal T cells and B cells through the production of cytokines. The function of immune cells is affected by aging. This can increase the risk of infectious diseases, reduce the antibody response to vaccination, and reduce the strength of immune cells to protect the body (5,6). Research has shown that exercise directly affects the immune system by strengthening the immune and antioxidant systems and anti-inflammatory effects, and indirectly by improving mood. In the case of coronavirus, a cytokine storm occurs, which disrupts the function of tissues such as the lungs, which may be exacerbated and exacerbated by exercise (7).

Results: It is recommended to follow a regular exercise program with an average of 20-30 minutes a day to strengthen the immune system and reduce the risk of viral infections. During moderate-intensity activity, the antipathogenic activity of tissue macrophages increases as the number of immunoglobulins, anti-inflammatory cytokines, NK cells, and immature B cells increases(8,9). This type of exercise is considered a treatment method due to its anti-inflammatory effects, which are effective in improving many diseases. Overall, research shows that if you exercise for more than 300 minutes a week at moderate intensity, it has anti-inflammatory effects and protects the body against viral infections such as Covid-19. Also, the use of herbal medicines is increasing in different countries due to growing concerns about the side effects of chemical drugs (10,11). Among these herbs, nigella extract has anti-inflammatory and immune-boosting effects that have led to many pharmacological effects (12). According to research, the use of black seed oil for four weeks causes a 55% increase in the ratio of CD4 + and CD8 + cells and a 30% increase in the function of NK cells (13).

Conclusion: Lifestyle changes are one of the newest recommended ways to improve and strengthen the immune system. As mentioned, having a daily exercise program, preferably with moderate intensity, can play an effective role in boosting the immune system. Unfortunately, the general public today does not value such sports programs due to lack of awareness, low level of social knowledge, and unfavorable conditions around them. Avoid smoking, avoid alcohol (even low alcohol consumption), get enough sleep, and maintain good public health are some of the factors that improve immune function.

Keywords: menopausal women , hot flashes , coronavirus , Covid-19 , vasomotor

Evaluating the effect of supernatant bacteria , Bifidobacterium bifidium on bcl-2 and bax gene expression in Testicular cancer cells (Research Paper)

Anoosheh Soleimani Rahim Abadi,[1,*] Mahnaz Farahmand,[2]

1. Department of biology,East Tehran Branch,Islamic Azad University
2.

Introduction: Men between the ages of 15 and 34 are at risk for testicular cancer. Men over the age of 55 are much more likely to develop testicular cancer. Spermatocystic type of testicular cancer occurs in men over 50 years of age. Today, bacteria such as bifidobacterium and Lactobacillus are recognized as a preventative factor in many diseases, including cancer. One out of every 250 men develops testicular cancer during their lifetime. Its maximum prevalence is between 20-40 years old. In fact, it is the most common cancer in men aged 20-40 years. Testicular cancer accounts for one percent of all malignancies in men. In about 2-3% of cases, testicular cancer is bilateral. Approximately 99% of hard masses inside Testicular tissue is cancer. 1-2% of testicular cancers are familial. Chemotherapy is one of the most effective treatments for testicular cancer. Early diagnosis such as clinical examination, tumor marker levels, and ultrasound are important for the survival and comfort of most patients. Factors that can be effective in the occurrence of this complication are abdominal testis, family history, race, infertility. In the Aryan race, the incidence is less. With a family history in first-degree individuals, the risk of testicular cancer increases tenfold.

Methods: First, bifidobacterium bifidium supernatant was prepared in different volumes of 7.81, 15.6, 31.25, 62.5, 125, 250, 500 µl of cell suspension in a volume of 1200 µl of cell culture medium Finally, the effect of bifidobacterium bifidium supernatant at pH 4 and 7 on testicular cancer cell line TM4 and on healthy testicular cells with neutral pH was investigated by MTT assay. Testicular cancer cell survival was calculated. The expression of two genes involved in BAX and BCL-2 cancer was evaluated after supernatant effect by Realtime PCR.

Results: Treatment of testicular cancer cells with different volumes of probiotic suspension showed that at higher volumes and time, the rate of cytotoxicity was higher and the survival rate of cancer cells decreased while it was not dependent on pH. There was no change in the effect of neutral pH supernatant on healthy cells. The lethal effect of 24h supernatant at PH4 at concentrations of 7.81, 15.6, 31.25, 62.5, 125, 250, 500 µl / ml on testicular cancer cell TM4, 27.5, 38.19, 58.77, 62.7, 73.7, 85.7, 92.68%, respectively. was observed. The lethal effect of 24h supernatant at PH7 at concentrations of 7.81, 15.6, 31.25, 62.5, 125, 250, 500 µl / ml on testicular cancer cell TM4,

25.8, 36.28, 56.74, 61.8, 71.79, 83.28, 92.52%, respectively. was observed. The lethal effect of 48h supernatant at PH4 at concentrations of 7.81, 15.6, 31.25, 62.5, 125, 250, 500 µl / ml on testicular cancer cell TM4, 33.28, 40, 63.85, 68, 81.49, 87, 95.88%, respectively was observed. The lethal effect of 48h supernatant at PH7 at concentrations of 7.81, 15.6, 31.25, 62.5, 125, 250, 500 µl / ml on testicular cancer cell TM4, 34.15, 41.87, 61.73, 69.63, 80.76, 88.9, 95.79%, respectively. was observed. The lethal effect of 72h supernatant at PH4 at concentrations of 7.81, 15.6, 31.25, 62.5, 125, 250, 500 µl / ml on testicular cancer cell TM4, 44.8, 53.68, 69.1, 73.1, 82.77, 90.8, 97%, respectively. was observed. The lethal effect of 72h supernatant at PH7 at concentrations of 7.81, 15.6, 31.25, 62.5, 125, 250, 500 µl / ml on testicular cancer cell TM4, 47.1, 52.2, 67.05, 72.18, 83.32, 91.25, 96.63%, respectively. was observed.Also, BAX cancer inhibitor gene increased compared to GAPDH control gene and BCL-2 gene decreased compared to GAPDH control gene.

Conclusion: In this study, the probiotic effect of Bifidobacterium bifidum on TM4 cancer cells was investigated and the results showed that Bifidobacterium bifidum supernatant has the ability to inhibit the growth of testicular cancer cells. In 1995 in vitro studies by Laurent Baricault examined the effect of fermented milk with 4 different probiotic bacteria separately on HT29 cancer cells (rectal cancer cells) and found that Bifidobacterium and L. helaventicus had the greatest effect on inhibiting cell growth. He had cancer and suggested that up to 50% of the growth of cancer cells may be that the production of these bacteria can affect the growth and differentiation of cells . In a 1997 study by Biffi on the inhibitory effect of 5 different species of lactic acid bacteria on breast cancer cells (MCF7), it was observed that all 5 species of Bifidobacterium infantis, Bifidobacterium bifidum, Bifidobacterium animalis, Lactobacillus acidophilus, Lactobacillus growth Cancer had an inhibitory effect and the greatest effect was related to Lactobacillus acidophilus and Bifidobacterium infantis It inhibited the growth of cancer cells by up to 85%. It also showed that the presence of bacteria themselves did not have a live effect and attributed the reason for this action to the production of anti-tumor and anti- tumor and anti-cancer compounds by these bacteria . In general, it can be said that the effective mechanisms in inhibiting the growth of TM4 cancer cells by Bifidobacterium bifidum compounds are not fully understood, but according to previous studies in similar cases, it can be said that these bacteria produce anti-tumor and anti-cancer compounds that can Involve in the growth and differentiation of cancer cells and prevent their growth. According to the results, it was observed that supernatant 72 had the greatest effect, which could be due to the higher amount of metabolites produced in the supernatant . In 2006, Vander Meulen stated that as the number of bacteria increases, so does the amount of material they produce, and in the constant phase the amount of these metabolites is constant.

Keywords: Bifidobacterium, bifidum , MTT, Realtime PCR, Testicular cancer

Evaluating the effects of topical administration of probiotics after SRP on periodontal condition in patients with moderate to severe chronic periodontitis - a randomized clinical trial (Research Paper)

Naser Sargolzaei,[1] Kimia Kelidari,[2] Negin Riahi,[3,*] Negar Bahrami,[4] Milad Bonyatpour,[5]

1. Department of periodontitis, College of dentistry, Mashhad University of medical sciences, Mashhad, Iran
2. Student Research Committee, Faculty of Dentistry, Mashhad University of Medical Sciences, Mashhad, Iran
3. Student Research Committee, Faculty of Dentistry, Mashhad University of Medical Sciences, Mashhad, Iran
4. Student Research Committee, Faculty of Dentistry, Mashhad University of Medical Sciences, Mashhad, Iran
5.

Introduction: Periodontitis is an infection-driven inflammatory disease of teeth surrounding tissues. The presence of pathogenic bacteria, the susceptibility of the host and the absence of beneficial bacteria are its main ethological factors. Oral hygiene instructions, scaling and root planning (SRP), antibiotics and surgery are the existing therapeutic techniques which only target the first two factors and are not long-lasting. Thus, researchers are looking for a medicament by using beneficial bacteria. The chosen method is to employ probiotics, which are bacteria with beneficial effects for humans because of their anti-microbial and anti-inflammatory effects. Several studies proved the efficacy of probiotics in the treatment of periodontitis, but only a few studies evaluated the effect of probiotics in the treatment of chronic periodontitis. Given that none of these studies have been carried out in Iran and several risk factors including genetics, environmental and behavioral factors are associated with periodontal diseases, the necessity of conducting such a study in Iran is of high importance. The aim of this study, therefore, was to evaluate the effects of probiotic administration as mouthwash after SRP on periodontal condition in patients with moderate to severe chronic periodontitis.

Methods: In this study which was a double-blinded randomized clinical trial, 51 eligible patients with moderate to severe generalized chronic periodontitis who were referred to dental clinics in Mashhad, Iran, were randomly allocated to two treatment groups (test and control). All the subjects were given 20 capsules (dissolved in water and used as mouthwash) similar in shape after receiving SRP and oral hygiene instructions. These capsules contained probiotic (FamiLact) in the test group, and in the control group they were placebo. At the initial phase of the study we used clinical attachment loss (CAL) in order to determine moderate to severe generalized chronic

periodontitis. Afterwards, we employed bleeding on probing (BOP) and pocket probing depth (PPD) before and after the 20-day course of treatment.

Results: Before therapeutic interventions, there was no statically significant difference in study indicators (age, gender, BOP, PPD). After the baseline treatments and the 20-day period of administration of the capsules, the test group demonstrated a 34.7% reduction in BOP index, and a 28.7% reduction was observed in the control group (P-value= 0.001, difference= 6%). The test group also showed a 1.68 mm reduction in PPD index which was significantly higher than that of the control group with 0.88 mm reduction (P-value=0.0001, difference= 0.79 mm).

Conclusion: According to the significant difference of treatment results between our two studied groups, it is concluded that topical administration of probiotics after SRP can help reduce periodontal inflammation by changing the subgingival microflora in patients with chronic periodontitis at least in the short-term.

Keywords: Chronic periodontitis, Gingiva, Scaling and root planning, Probiotic, Oral health

Evaluating the relationship between RANK rs1805034 SNP and the serum levels of RANK protein as a predictive marker of heart diseases in patients with Beta-Thalassemia Major Running Title: Heart Iron Overload in Thalassemia Major (Research Paper)

Mojtaba shafiei,[1] Leila Noorazar,[2] Mohammadreza keramati,[3,*]

1. Hematology and blood banking Mashhad university of medical science , Mashahd , Iran
2. Hematology and blood banking Beheshti university of medical science , Tehran,Iran
3. Cancer molecular pathology research center, faculty of medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

Introduction: Background: Beta-thalassemia major is one of the well-known genetic disorders worldwide. Due to regular blood transfusions, iron deposition in the heart tissue results in cardiovascular diseases in beta-thalassemia patients. RANK/RANKL/OPG axis is a well-known signaling pathway that possesses a pivotal role in osteogenesis. The relationship between various single nucleotide polymorphisms (SNPs) of genes and cardiovascular diseases has been reported frequently. In this study, we surveyed the effect of RANK rs1805034 SNP and the RANK serum levels in patients with beta-thalassemia major on cardiovascular diseases.

Methods: Material & methods: This case-control study was performed on 80 patients with a beta-thalassemia major who referred to Mashhad Sarvar Clinic, Mashhad, Iran between Jun and November of 2018, and 80 sex- and age-matched healthy people as the control group. All patients were examined by two-dimensional echocardiography, M-Mode Doppler, and T2*MRI. The rs1805034 gene polymorphism of RANK gene was analyzed by the Sanger sequencing method. The serum levels of RANK were evaluated by ELISA. Left ventricular hypertrophy (LVH) and diastolic dysfunction (DD) were detected in 33 (41.25%) and 36 (45.0%) patients, respectively.

Results: Our results showed that patients with RANK rs1805034 SNP were not at high risk for LVH and diastolic dysfunction. No significant association between this SNP, LVH, and DD was observed. The serum levels of RANK were not associated with LVH, DD, and T2*MRI indexes in these patients.

Conclusion: In general, we did not find any significant correlation between RANK rs1805034 SNP and cardiovascular diseases in beta-thalassemia major patients.

Keywords: RANK, SNP, T2*MRI, Left ventricular hypertrophy, Thalassemia Major

Evaluation of apoptosis induction in HCT 116 cell line treated with curcumin encapsulated in nano-niosomes (Research Paper)

Navid Mousazadeh,[1] Mahmoud Gharbavi,[2] Hamid Rashidzadeh,[3] Hamed Nosrati,[4] Hossein Danafar,[5] Behrooz Johari,[6,*]

1. Department of Medical Biotechnology, School of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran
2. Department of Pharmaceutical Biomaterials, School of Pharmacy, Zanjan University of Medical Sciences, Zanjan, Iran
3. Cancer Gene Therapy Research Center, Zanjan University of Medical Sciences, Zanjan, Iran
4. Department of Pharmaceutical Biomaterials, School of Pharmacy, Zanjan University of Medical Sciences, Zanjan, Iran.
5. Cancer Gene Therapy Research Center, Zanjan University of Medical Sciences, Zanjan, Iran
6. Department of Medical Biotechnology, School of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran

Introduction: Among various types of cancer, colorectal cancer (CRC) ranks third in terms of incidence but second in mortality (1). Chemotherapy, surgery, and radiotherapy are common methods of treatment of CRC (2). Emergence of drug resistance and severe drug toxicity associated with chemotherapeutics have dramatically restricted the successful treatment of cancer disease, thus in this context wise steps should be taken to tackle these problems. Dietary phytochemicals are promising options in cancer therapy owing to their potential in cancer prevention and growth inhibition. Curcumin (CUR) is a dietary phytochemical found in Curcuma longa and has presented a broad range of biological activities, such as anti-oxidant, anti-malarial, anti-inflammatory and anti-cancer effects and exhibited great anti-cancer activity against a variety of different malignancies (3-5).Furthermore, CUR has displayed good pharmacological properties, but due to low absorption, rapid metabolism, low bioavailability and degradability in alkaline conditions have limited its therapeutic application (5). In this regard, researchers have devoted substantial efforts to improving its therapeutic efficacy. One promising approach to overcome the aforementioned drawbacks is using nanotechnology based drug carriers.. Niosomes (non-ionic surfactant vesicles) as an effective novel drug vehicles have been applied to deliver different types of bioactive compounds such as peptides, antigens, hormones, genes and chemotherapeutics (6).The most remarkable feature of niosomes is capability of loading both lipophilic and hydrophilic drugs in which lipophilic one entrapped in membrane bilayer of niosome whereas hydrophilic drugs entrapped into the aqueous core (7). Of note, the benefits of niosomes have not been ended just with the aforementioned advantages, other striking strengths are biodegradability, low toxicity, biocompatibility and non-

immunogenicity (8). Within the framework of the above mentioned criteria we aimed at preparing niosome loaded CUR and investigate its potential in induction of apoptosis against human colorectal cancer cell lines HCT116 and compared its efficacy to free CUR

Methods: HCT116 cells were maintained in DMEM High Glucose with 10% fetal bovine serum, penicillin and streptomycin. Typically, HCT116 cells were cultured and incubated in a %5 CO2 atmosphere at 37°C. In brief, HCT 116 cells were seeded in a 12-well plate, and once the confluency of HCT116 cells reached to the desired amounts, they were treated with the different groups and after incubating for 24 hours; cellular apoptosis was assessed by flow cytometry. It should be noted that the CUR loaded niosomes were prepared by thin-film hydration method and their size was determined by dynamic light scattering (DLS) technique. Standard curve of CUR was obtained by measurement the absorption peak of free CUR at wavelength of 428 nm at different concentrations. All attained data were expressed as the mean ± SD (standard deviation).

Results: DLS measurement indicated that the hydrodynamic diameter of the fabricated niosomal formulation was below 100 nm. In this study, cells were treated with free CUR, blank niosomes and CUR loaded niosomes and after 24 hours of incubation the cell apoptosis were investigated using flow cytometry technique. It was found that both free CUR and CUR loaded niosomes at the same concentration (40 μM) could significantly induce apoptosis in HCT116 cell line. The percentage of apoptosis for free CUR, blank niosomes and CUR loaded niosomes were 16.83 ± 1.50, 5.50 ± 0.87 and 23.80 ± 2.29, respectively

Conclusion: In this study, HCT 116 colon cancer cells were treated with both free CUR and CUR loaded niosomes, and cell apoptosis results showed that the CUR loaded niosomes exhibited significantly higher cell apoptosis than free CUR, which indicating the importance role of using nanocarriers in induction of apoptosis. On the other hand, blank niosomes did not induce significant apoptosis compared to control group and outlining the fact that the fabricated niosomes as a drug vehicles are suitable and practically non-toxic. Overall, nanocarrier-based drug delivery systems can play an important role in inducing cellular apoptosis, but more comprehensive studies should be conducted in this regard to fully elucidate these findings.

Keywords: Cancer,Niosomes,Curcumin,Colon cancer,apoptosis

Evaluation of adherence of vibrio cholera Non-O1/Non-O139 to HT-29 cell line (Research Paper)

Jafar Alinezhad,[1] Mohammad Ali Haghighi,[2,*] Somayyeh Gharibi@gmail.com,[3] Omid Rasoolzadeh,[4]

1. Student Research Committee, Bushehr University Of Medical Sciences, Bushehr, Iran
2. Department of Microbiology and Parasitology, School of Medicine, Bushehr University of Medical Sciences, Bushehr, Iran
3. Department of Microbiology, School of Sciences, Kherad Institute of Higher Education, Bushehr, Iran
4. Student Research Committee, Bushehr University Of Medical Sciences, Bushehr, Iran

Introduction: Successful establishment of infection by vibrio cholerae requires adhesion to the intestinal mucus barrier. Human adenocarcinoma-derived intestinal cell lines offer easy and elegant ways to study bacterial adherence to the intestinal. This study was aimed to understand the adherence rate of Vibrio cholerae to HT-29 cell line.

Methods: The adhesion assay was performed on HT-29 cells and cultured in 12-well dishes .HT-29 cells were grown to confluence in DMEM containing 10% FBS and washed with PBS, and DMEM without FBS was added. V. cholerae cultures grown to the midexponential phase in LB were suspended in DMEM added to the HT-29 monolayer at different multiplicity of infection (MOI), and incubated for 45 min at 37°C in a 5% CO2 atmosphere. After 45 min the number of cfu of adhered bacteria was calculated.

Results: The adhesion strongly increased after 45 min of V. cholerae exposure to the HT-29 cell at 37 ° C in MOI 35. In the case of the highest MOI, the number of adhered bacteria was lower for adherence analyzed after the count compared to the MOI 35.

Conclusion: Bacterial attachment and host colonization are key events in V. cholerae infection and result in the ability of the infecting bacterial cells to persist and multiply. In this study, we sought to determine inoculation of which number of V. cholerae provides the best adhesion. Decrease amount of adherence was in highest MOI shows that adherence could be in a concentration-dependent manner. The results of adherence analysis were indicative of this.

Keywords: Vibrio cholerae, Adherence Assay, HT-29

Evaluation of antibacterial and antioxidant activity of betamethasone polymeric nanofibers against bacterial skin infections: in vitro analysis (Research Paper)

Fatemeh Ashrafi,[1,*] Pooria Moulavi,[2] Minoo Sadri,[3]

1. Phd of Microbiology, Islamic azad university, North tehran branch, Tehran, Iran
2. Department of Biology, Tehran North Branch, Islamic Azad University, Tehran, Iran
3. Department of Biochemistry and Biophysics, Education and Research Center of Science and Biotechnology, Malek Ashtar University of Technology, Tehran, Iran.

Introduction: Skin and soft tissue infections (SSTIs) are among the most prevalent sorts of infections, with a wide range of etiologies and manifestations. Globally, the prevalence of SSTIs is larger than that of urinary tract infections and pneumonia combined, and it is constantly increasing. Skin infections have been associated with a multitude of organisms, which include Gram-positive and Gram-negative bacteria, fungi, and yeasts. It is therefore critical to assess alternative antimicrobial agents and therapeutic methods that target bacteria implicated in skin infection. Electrospinning is a flexible process for producing fibers with nanoscale micrometer diameters, significant oxygen permeability, variable pore diameters, and a substantial surface area ratio that is morphologically comparable to the extracellular matrix. As a result, electrospun nanofibers are suitable as wound dressing materials. Numerous chemicals have been electrospun into nanofibers to regulate their release. The purpose of the present survey was to analyze the feasibility of electrospinning commercially available betamethasone into nanofibers comprising of a mixture of honey, poly (ethylene oxide) (PEO), and Polyvinyl alcohol (PVA) to evaluate antimicrobial effects against skin infections.

Methods: At the first, for the synthesis of PEO / PVA / honey nanofibers containing betamethasone, all three polymer solutions of 12% PEO, 7% PVA, and 12% honey were prepared separately, and then a certain amount of drug was blended with polymers solution for the synthesis of polymer nanofibers containing 10% and 5% of betamethasone. The solution of the nanofibers containing10% of betamethasone was then placed in an electrospinning device under electrospinning conditions (25G, 0.1 cc/h Discharge Per Polymer, 15 cm, 10.5 kV). Finally, the obtained fibers were investigated by light microscopy (X40). The antibacterial effects of synthesized nanofibers were also investigated against skin infection bacteria including Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa, Escherichia coli, and Proteus mirabilis using well diffusion, disc diffusion, minimum inhibitory concentration (MIC), and minimum bactericidal

concentration (MBC) methods. The antioxidant capacity of IC50 concentrations of betamethasone-loaded polymeric nanofibers was assessed using an in vitro detection of intracellular reactive oxygen species generation in skin cancer cells

Results: The results of the current study showed that polymeric nanofibers containing different concentrations (5 and 10%) of betamethasone were well synthesized by the electrospinning method. Also, the antibacterial properties of synthesized nanofibers containing betamethasone were confirmed by MBC, MIC, well diffusion, and disc diffusion methods on the standard microbial strain involved in skin infections. The results of antibacterial tests also showed that nanofibers containing betamethasone had a 10% similar effect to gentamicin and this behavior was concentration-dependent. The results of antibacterial tests also showed that nanofibers containing betamethasone 10% had a similar effect to gentamicin and this behavior was concentration dependent; the strains treated with 5% betamethasone-polymeric nanofibers generated a smaller halo diameter than strains treated with gentamycin and 10% betamethasone-polymeric nanofibers. The most sensitive strain against synthesized nanofibers was the standard strain of Escherichia coli; however, the standard strain of Pseudomonas aeruginosa exhibited the highest resistance to these nanofibers. Antioxidant tests showed that the IC50 concentration of betamethasone-loaded polymeric nanofibers (283.22 µg/ml) had a greater ability to eliminate reactive oxygen species (ROS) than betamethasone alone (423.1 µg/ml) .

Conclusion: In conclusion, betamethasone was propitiously electrospun into honey/PEO/PVA nanofibers, and released betamethasone was capable to prevent the growth of standard strains of Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa, Escherichia coli, and Proteus mirabilis over a lengthened period of time. This formulation also is a proper antioxidant candidate against ROS in skin cancer treatment. Betamethasone-containing honey/PEO/PVA nanofibers may thus be appropriate wound dressing substances to decrease the bacterial burdens of infected skin wounds. Further investigation should focus on combining growth factors, anti-inflammatory drugs, and analgesics, as well as other possible antimicrobials agents to develop an ideal wound dressing that can treat infections and minimize the time required for wound healing.

Keywords: Antibacterial, Anti-oxidant, Electrospanning, Betamethasone, Skin bacterial infections

Evaluation of antibacterial function of liposomes containing aloe vera extract by Mozaffari method (Research Paper)

Maryam Cheshmberah,[1] Mohammad Javad Forouzani-Moghaddam,[2,*]

1. MSc of Genetic, Sistan & Balochestan university, Zahedan, Iran
2. Msc of Food Microbiology, School of Paramedical, Iran University of Medical Sciences, Tehran, Iran

Introduction: The aim of this study was to investigate the antibacterial function of liposomes containing aloe vera extract. For this purpose, liposomes containing aloe vera extract have been synthesized for optimal use against Staphylococcus aureus and Escherichia coli.

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 a DLS device and morphology with an atomic energy microscope (AFM) and the amount of loading and release with a spectrophotometer. MIC tests were then performed to evaluate the performance of nanoparticles containing aloe vera extract on Staphylococcus aureus and Escherichia coli.

Results: The mean particle diameter was 72 nm and its zeta potential was 14 mV. The loading rate in nanoparticles was 60%, which was calculated by reading the absorption of light from the standard Zanian curve. The minimum inhibitory concentration (MIC) of Staphylococcus aureus and Escherichia coli for nanoparticles was 62.5 and 125 mg / ml.

Conclusion: Nanoparticles containing aloe vera extract kill the bacterial bacteria Staphylococcus aureus and Escherichia coli and can be used as antibacterial nanosystems.

Keywords: Aloe Vera, Antibacterial, Staphylococcus aureus, Escherichia coli

Evaluation of antimicrobial effect of probiotics isolated from Gilan province traditional milks against Candida albicans as well as Pseudomonas aeruginosa and comparision with standard probiotics strains. (Research Paper)

Moayed Atashak,[1,*] Mahnaz Farahmand,[2] Elaheh Ali Asgari,[3]

1. Department of biology, Basic Science Faculty, East Tehran Branch, Islamic Azad University, Tehran, IRAN.
2. Department of biology, Basic Science Faculty, East Tehran Branch, Islamic Azad University, Tehran, IRAN.
3. Department of biology, Basic Science Faculty, East Tehran Branch, Islamic Azad University, Tehran, IRAN.

Introduction: Probiotics are alive microorganisms which are added to human and animal diet for improving and correcting bacterial flora; probiotics are able to restrain unwanted colonization of pathogens in the digestive system. Additionally, probiotics are capable of eliminating pathogens through secreting various bacteriocin materials such as Acetate, Propionate, and Hydrogen peroxide. Candida albicans is a species of yeast which lives in symbiotic relationship with the skin, oral, gut, and vagina of its host. In normal conditions, C.albicans do not cause harms to their host, but the tension of the immune system creates the opportunity for it to manifest itself as a pathogen. Pseudomonas aeruginosa is a similar opportunist microorganism that in case of immune system weakness results in several types of infections including - but not limited to - urinary track, respiratory system, and gastrointestinal infections, particularly in patients suffering from cancer or HIV. Therefore, due to the range of diseases that these pathogens have caused for human beings, and arbitrary consumption of antibiotics that has increased their resistance to old-fashioned medications, finding new ways which are safe, permanent, and available seems necessary. Considering the variety of detriments caused by the aforementioned pathogens and the medical benefits of probiotics, we aimed to identify probiotics from local milk for potential use against C.albicans and P.aeruginosa.

Methods: To begin with, 10 milk samples were collected from different areas of Gilan province. Then, each sample was cultured as well as incubated in MRS Broth medium. Afterwards, for removing the unwanted microorganisms, acidity tolerance and bile site tolerance tests were performed. Microorganisms which could tolerate the conditions were cultured in MRS Agar and were incubated. In the following, to identify the characteristics of those microorganisms, tests such as gram stain, catalase, and carbohydrate fermentation were carried out. In order to detect the microorganisms, first, their DNA's were extracted through DNA-extraction kit, and then, PCR for 16s rRNA was conducted. Eventually, to measure the effects of harvested

probiotics against P.aeruginosa and C.albicans, the well-diffusion method was used. To do so, first, criterion species of C.Albicans (PTCC 5027) and P.aeruginosa (PTCC 1690) were cultured and standard dilution was prepared. Then, the standard dilution of pathogens was inoculated on solid culture medium, and a hole was made in the center of the culture medium. The next step was to prepare a standard dilution of probiotics which was harvested from milk samples, and 50 to 70 µl was added to the hole. This test was reperformed with the difference that this time the standard strain of probiotics was used rather than the harvested one. Finally, samples were incubated for analyzing the results.

Results: Our results indicated that the grown colonies which harvested from milk were the same size, white in color, and were gram positive cocci. Likewise, the result of catalase test was negative, and the results of acidity and bile-salt tests prove that almost %37 of microorganisms tolerated this condition. From nine carbohydrate which were used, the harvested probiotic was capable to ferment six of them including Lactose, Maltose, Mannitol, Ribose, sorbitol, and Glucose, while Arabinose, Inulin and Raffinose were not fermented. Isolated probiotics were over than %99 similar to Enterococcus Faecalis. Effects of both isolated E.Faecalis and standard strain of E.faecalis showed no harmful impact on C.albicans. At the same time, comparing with C.Albicans, P.aeroginosa was sensitive to E.faecalis. Similarly, standard strain of E.Faecalis and isolated E.Faecalis showed zone of inhibition with diameter of 3.13 mm and 3.86 mm, respectively. Still, there were no observation of P.aeruginosa colonies.

Conclusion: According to our results, we realized that despite the fact that P.Aeruginosa was sensitive to E.Faecalis, C.Albicans showed resistance to E.Faecalis. We also found out that isolated E.Faecalis was more effective in proportion to its standard strain. An interesting point in this study was that different types of probiotics can be effective for eliminating pathogens, unlike other species. Thus, we suggest to test a range of probiotics against quite a few types of pathogens. By doing so, we can use probiotics to purposefully treat infections caused by a specific pathogen, or identify their useful types and use them on food industry to reinforcing the immune system.

Keywords: Probiotics, C.albicans, P.aeroginosa.

Evaluation of application zinc nanoparticles with chitosan biofilm on healing of infected wound with methicillin-resistant Staphlococcus aureus (MRSA) in rat (Research Paper)

Leila Zarei,[1] Asghar Rajabzadeh,[2,*]

1. .Associate Professor,Department of Anatomical Sciences, Faculty of Medicine, Lorestan University ofMedical Sciences, Khorramabad, Iran.
2. Assistant Professor,Department of Anatomical Sciences, Faculty of Medicine, Lorestan University ofMedical Sciences, Khorramabad. Iran.

Introduction: The present study was aimed at assessment of effect of application of zinc nanoparticles with chitosan biofilm on healing of infected wound with Methicillin- resistant Staphylococcus aureus (MRSA) in rat.

Methods: Sixty-eight male Wistar rats were randomized into four groups of 17 animals each. In group I (Normal) the wounds were created with no infection. In group II (CHIT), the wounds with no infection were dressed by chitosan biofilm. In group III (MRSA/CHIT), animals with infected wounds were dressed with chitosan biofilm only. In group IV (MRSA/CHIT/NZ), animals with infected wounds were dressed with Chitosan/Nano zinc biofilm.

Results: There were significant differences in comparisons of group IV and other groups, particularly in terms of cellular infiltration and neovascularization. During the study period, scores for neovascularization was significantly higher in group IV rats than other groups ($P < 0.05$). Polymorphonuclear (PMN) and mononuclear (MNC) cell count and fibroblast cell proliferation in group IV were significantly higher than those of other experimental groups ($P < 0.05$).

Conclusion: Chitosan/Nano zinc biofilm resulted in significant improvement in histopathological indices in full thickness infected wound healing.

Keywords: Infected wound, Chitosan/Nanozinc, biofilm, rat

Evaluation of CD34+ Cell Count at Different Time Points following Plerixafor Administration in Autologous Hematopoietic Stem Cell Transplantation (Research Paper)

Leila Noorazar,[1] Mojtaba Shafiei,[2] Majid Gholizadeh,[3] Sayeh Parkhideh,[4,*]

1. Hematopoietic stem cell research center, shahid beheshti university of medical sciences, Tehran, Iran
2. Mashhad University of Medical Sciences Faculty of Medicine, hematology and blood banking Mashhad, Razavi Khorasan, IR
3. Shahid Beheshti University of Medical Sciences, Department of Hematology and Blood Banking, School of Allied Medical Sciences Tehran, IR
4. Hematopoietic stem cell research center, shahid beheshti university of medical sciences, Tehran, Iran

Introduction: Introduction: In apheresis, collecting an adequate number of CD34+ cells is required for successful autologous hematopoietic stem cell transplantation (auto-HSCT) procedure. It is difficult to harvest a sufficient number of stem cells in certain patients due to their old age and history of intensive chemotherapy. Plerixafor could mobilize stem cells and facilitate peripheral blood hematopoietic stem cell collection. However, not enough information is available at the appropriate time intervals from plerixafor administration to apheresis.

Methods: Methods: Circulating CD34+ cells were enumerated by flowcytometry on day 4 post mobilization. Plerixafor was administered to patients with poor mobilization based on the count of peripheral blood hematopoietic stem cells. The number of circulating CD34+ cells was evaluated before and 3, 6, 9, and 12 hours after plerixafor administration to assess the time it takes for stem cells to reach their peak level.

Results: Results: The highest level of stem cell concentration was found in 9 h after plerixafor administration with an increasing trend. A statistically significant relationship was also observed between factors including platelet count on the first day of GCSF injection and the day of stem cell infusion, leukocyte count on admission, and basal levels of CD34+ cells in peripheral blood and the amount of harvested stem cells.

Conclusion: Conclusion: We demonstrated that plerixafor causes an incremental trend in CD34+ cells mobilization, reaching its peak after 9 hours. Further research should be performed to provide insights into graft cells' population and hematologic and immunological recovery.

Keywords: Apheresis, CD34+ cells, Mobilization, Plerixafor

Evaluation of clinical manifestations of 83 children with Covid-19 disease according to the symptoms approved by the Center for Disease Control and Prevention (CDC) (Research Paper)

Seyed Mohsen Laal Mousavi,[1] Homa Hajizadegan,[2] Reza Khoshbakht,[3,*] Fatemeh Zahra Karimi,[4] Elahe Saberi Teymourian,[5]

1. Department of Health Information Technology, Faculty of Paramedical, Mashhad University of Medical Sciences, Mashhad, Iran.
2. Department of Health Information Technology, Faculty of Paramedical, Mashhad University of Medical Sciences, Mashhad, Iran.
3. Department of Laboratory Sciences, Faculty of Paramedical, Mashhad University of Medical Sciences, Mashhad, Iran.
4. Department of Laboratory Sciences, Faculty of Paramedical, Mashhad University of Medical Sciences, Mashhad, Iran.
5. Department of Laboratory Sciences, Faculty of Paramedical, Mashhad University of Medical Sciences, Mashhad, Iran.

Introduction: Background: The coronavirus disease 2019 (COVID-19) is quickly spreading throughout the world. It discovered that COVID-19 caused severe endemic and epidemic pneumonia, with quick deterioration to acute respiratory distress syndrome (ARDS) and significant mortality in individuals. According to reports, in comparison to adults, the prevalence of serious illnesses and death among children is extremely low. Other findings suggest that, as with other respiratory viruses, transmission from children may play a major role in the spread of SARS-CoV-2. Despite its epidemiological significance, the clinical features of children infected with Covid-19 are unknown. The purpose of this study was to investigate the clinical manifestations of children infected with Covid-19.

Methods: Methods: The study was performed on 83 children under 18 with Covid-19 from March 2020 to September 2020 (6 months). Definite infection in these children was determined by PCR test and patients were evaluated for symptoms presented by the report of the symptoms according to CDC. Data were analyzed by SPSS 16 software and Chi-square statistical test.

Results: Findings: A total of 83 children with Covid-19 disease were included in this study. Of these cases: 53% (n=44) were females. The most prevalent symptom was respiratory distress syndrome (n=42, 50.6%), fever (n=25, 30.1%), followed by cough (n=24, 28.9%). Statistical test of patient's symptoms in different age groups in children has shown there was no significant difference between the age group and none of the symptoms (P-value> 0.05). As a result, the hypothesis of an association between age groups and symptoms observed in each age group was rejected.

Conclusion: Conclusion: The results of our study showed that there was no significant relationship between the age groups of children under 18 years old and Covid-19 disease. In general, the clinical signs of the disease in children were similar to those of adults mentioned in the reference sources. However, due to the possibility of symptoms affecting the child's growth as well as unknown complications, it seems necessary to pay attention to timely treatment.

Keywords: Keywords: CDC, COVID-19, Child, Symptoms and Signs

Evaluation of dairy –derived Streptococcus Thermophilus on the IL-17/IL-23 axis in A549 Cancer Cells (Research Paper)

Forugh Perotta ,[1] Fereshteh Kabi ,[2] Safoura Sameni ,[3,*] Elham Moazamian ,[4]

1. Department of Biochemistry, Shiraz Branch, Islamic Azad University, Shiraz, Iran
2. Department of Microbiology, Shiraz Branch, Islamic Azad University, Shiraz, Iran
3. Department of Biochemistry , Shiraz Branch, Islamic Azad University, Shiraz, Iran
4. Department of Microbiology, Shiraz Branch, Islamic Azad University, Shiraz, Iran

Introduction: Probiotics have the potential of improving the Immune system and are used to treat cancer. These bacteria stimulate and strengthen the immune system. The present study aims to evaluate the effect of Streptococcus Thermophilus bacteria metabolites on the immunological axis of IL17/ IL23 in A549 cancers cell.

Methods: A number of dairy-based bacterial samples were collected and isolated from Fars province, Iran. The isolated metabolites of the Streptococcus Thermophilus strain were then added to the A549 lung cancer cell cultures and the fluctuation of the produced IL17/ IL23 levels were examined by the ELISA test.

Results: It has been shown that dairies from different origins can affect the immunological axis of IL17/IL23 in different ways, leading to improvement or suppression of immune system in the cancerous environment.

Conclusion: In this study two of the isolated bacteria from dairy products of Fars province showed good performance against inflammation and A549 cancer cells which shows that the metabolites of the probiotic bacteria can be used to treat the cancer.

Keywords: Streptococcus Thermophilus, Lung cancer, Interleukin 17, Interleukin 23

Evaluation of genetic causes of recurrent miscarriage (Review)

Zahra Sadat Aghaei Shahri,[1,*]

1. Zahra Sadat Aghaei Shahri Member of the Research Committee of the Islamic Azad University of Mashhad. Iran

Introduction: Recurrent miscarriage (RM) is a common fertility complication that refers to three or more consecutive miscarriages that occur before the twentieth week of pregnancy. Chromosomes are located in a prokaryotic cell or in the nucleus of a eukaryotic cell and contain DNA. Genetic defects are caused by genetic mutations that occur in the fetus. Any detectable and inherited change in genetic material that causes a change in genotype and is passed on to daughter cells and future generations is called a mutation. Mutations may be inherited from the parent genome or created in the womb. Polymorphisms are regular and occur in a group between two or more discontinuous genotypes.

Methods: Articles reviewed in databases published from 2012 to 2021. Search by keywords recurrent miscarriage, genetic defects, chromosomes, polymorphisms, genetic mutations. 6 articles from google scholar database and 9 articles from database pubmed were selected. 4 articles from google scholar database and 6 articles from pubmed database were deleted due to lack of connection with the title of the items and finally 5 articles were reviewed.

Results: In 2 studies, it was found that chromosomal abnormalities of displacement and inversion play an important role in RM, which accounts for 50% of RM in the first trimester and affects the morphological y, y histology, and secretion of hormones and proteins. Put. Leads to hypoplasia, placental abruption, vascular disorders and eventually miscarriage. In 3 studies mutations in genes associated with Smith-Lamelie Opitz syndrome, congenital methemoglobinemia and sickle cell anemia, myotonic dystrophy, tanatophoretic dysplasia and type II osteogenesis imperfecta and methylene-tetrahydrofolate-reductase mutation (VA) M16 (TF) And factor II G20210A is mentioned which leads to RM. Based on 3 studies, we found that 53 genetic polymorphisms of 37 genes affect the creation (RM). Based on 2 studies, we found that genes associated with thrombophilia, cytokines, hormone receptors, and genes associated with angiogenesis are prone to RM, and abnormal placental function, hyperactive immune responses, and metabolic disorders are among the causes of RM. In 1 study found that NLRP2 or NLRP7 malfunction leads to RM. SNPs in some genes and overexpression of miRNAs (microRNA-575) can also cause RM.

Conclusion: Given that one of the most common causes of recurrent miscarriage can be genetic defects, chromosomes, polymorphisms, genetic mutations, and genetic problems and recurrent miscarriage threaten both couples. Therefore, in people who have had recurrent miscarriages, it is necessary to refer to a geneticist and check the chromosomes of man and woman by genetic testing and karyotype determination.

Keywords: Recurrent miscarriage, Genetic defects, Chromosomes, Polymorphisms, Genetic mutations

Evaluation of genetic pattern of the most common cause of recurrence of bacterial urinary tract infection in kidney transplant patients, Tehran, Iran (Research Paper)

Maryam Keshtvarz,[1,*] Mohammad Reza Pourmand,[2] Zahra Zareh,[3] Mohammad Ali Haghighi,[4]

1. Bushehr University Of Medical Sciences, Bushehr, Iran
2. Department of Pathobiology, School of Public Health, Tehran University of Medical Sciences
3. Bushehr University Of Medical Sciences, Bushehr, Iran
4. Bushehr University Of Medical Sciences, Bushehr, Iran

Introduction: Renal transplantation is the choice treatment for patients at end stage renal disease. Urinary tract infection (UTI) is one of the most common complications after renal transplantation, and it has serious consequences. Plused- Field Gel Electrophorsis (PFGE) is a new and accurate method for epidemiological studies of pathogenic organisms. The aim of this study was assessing UTI and recurrence in renal transplanted patients and used the PFGE method to obtain the genetic pattern of the most common cause of urinary tract infection and recurrence .

Methods: In this study, bacterial urinary tract infections in renal transplant recipients were determined.. The urine samples were taken from 94 hospitalized patients within 8-10 days after catheter removal and re-samples during the 6 months after transplantation for detection of recurrence , urinalysis and colony count were performed. Susceptibility of all the isolates to different antibiotics was determined by agar disk diffusion method and then the genetic patterns of the commonest isolated bacteria were obtained by PFGE and compared with patterns of antibiotic resistance.

Results: UTI was observed in 29 of patients and the most prevalent microorganism was E. coli 14(14.7%). Recurrence UTI occurred in 15(15.8%) patients and the main agent pathogen involved in recurrence was E.coli. Most of the isolated bacteria were susceptible to imipenem and resistant to Cotrimoxazole and Piperacillin. 13 patterns of antibiotic resistance and 13 DNA profiles in hospitalized patients and 14 patterns of antibiotic and 12 DNA profiles in outpatients were recognized.

Conclusion: Our study confirmed that bacterial infections remain as the most common infectious complication in the early post transplant period, and antibiogram rather than empirical treatment is needed to find the best effective antibiotics. With regard to high differentiation power of PFGE method, obtained patterns and high diversity of these profiles no epidemic UPEC was

determined in hospitalized patients and outpatients. So, our result suggest that the most of recurrence UTIs in renal transplant patients caused by the same isolates.

Keywords: Urinary Tract Infections, Renal transplantation, E. coli, PFGE

Evaluation of genetic variations in exon 10 of SPATA6 gene in infertile men with acephalic spermatozoa syndrome (Research Paper)

Seyedeh-Nadia Mahmoudi Nasrabadi,[1] Maryam Eslami,[2] Marjan Sabbaghian,[3,*]

1. Applied Biotechnology Research Centre, Tehran medical science branch, Islamic Azad university,Tehran, Iran.
2. Applied Biotechnology Research Centre, Tehran medical science branch, Islamic Azad university,Tehran, Iran.
3. Department of Andrology, Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR,Tehran, Iran.

Introduction: Acephalic spermatozoa syndrome is a one of the most severe forms of teratozoospermia which cause male infertility; it can be easily defined through detection of decapitated flagella, tailless sperm heads in the ejaculated. In this syndrome, the sperm's head is separated from the flagellum because there is a problem in head –tail junction. This condition was caused by a defect in the spermatogenesis stage in the testicle. It is an autosomal recessive type defect and probably has genetic implications in many cases. Furthermore, SPATA 6 (Spermatogenesis Associated 6) produces a testis-specific protein that localized in the mature spermatozoa head-to-tail linkage site and plays a role in the attachment of the head-tail of the flagellum during spermatogenesis. In this study we investigated the variations of exon 10 of SPATA6 gene in infertile men with acephalic spermatozoa syndrome.

Methods: In the present study, 8 infertile men with acephalic spermatozoa syndrome as a case group and 8 fertile men as a control group were recruited. DNA was extracted from peripheral blood and after designing primers, PCR reaction and sanger-sequencing were performed. The results of sequenced segments were analyzed by Finch TV and Blast

Results: Sequencing results revealed no genetic variations (mutations or single nucleotide polymorphisms) in men with acephalic spermatozoa syndrome and controls.

Conclusion: Despite the fact that in this study there is no relationship between the genetic variations of exon 10 of SPATA6 gene and acephalic spermatozoa syndrome, since SPATA6 is necessary for head- tail junction, it seems for a closer look it should be suggested to examine other exons in this gene, splice sites and the promoter.

Keywords: Male infertility, SPATA6 gene, Male infertility, Acephalic spermatozoa syndrome

Evaluation of knowledge, attitude and practice of pregnant mothers referring to Taleghani Educational and Medical Center regarding Covid -19 disease (Review)

Anahita Parsanezhad,[1,*]

1. Farzanegan high school of Tabriz (Sampad)

Introduction: Covid-19 disease is a contagious disease and its most important challenge is the threat to human health around the world. People's awareness and understanding of the risk and their actions in this critical situation play an important role in controlling the disease. Pregnant mothers as a vulnerable group in the community are at risk of developing the complication of Quid and this group is a major risk to community health. This study examines the knowledge, attitude and practice of pregnant mothers referring to Taleghani Center. Has dealt with Covid-19 disease and methods of prevention and control.

Methods: The present study is a descriptive cross-sectional study in which the knowledge, attitude and practice of 100 pregnant women referred to Taleghani Center about Covid-19 disease, by presenting a self-made questionnaire consisting of demographic information, 13 questions in the field of knowledge about The nature of the disease, the mode of transmission, symptoms and strategies for prevention and control and 3 questions about the role of the individual in the control and prevention of the disease and the study of beliefs and beliefs about the role of health protocols in preventing the disease and 12 questions in the field of function and The behavior of the research samples was evaluated and analyzed.

Results: The mean scores of knowledge, attitude and practice of pregnant mothers towards Covid- 19 disease were higher than average (96.2%), (89.6%) and (81%), respectively. There was a significant relationship between the level of education and the number of family members with the knowledge and practice of pregnant mothers about the disease, its prevention and control.

Conclusion: Findings from this study provided information about the level of knowledge, attitude and practice of pregnant mothers as individuals in high-risk and vulnerable groups in the Covid -19 crisis, due to the emergence of the disease, lack of sufficient knowledge about its prevention and treatment and The importance of maternal and fetal health in society, ongoing challenges to improve their awareness and proper practice in disease prevention and control by providing ongoing education and updating their

information with the latest knowledge in the world and providing the necessary facilities, is still emphasized.

Keywords: Disease - Covid 19 - Pregnant mothers

Evaluation of marital satisfaction of employed and non-employed couples from marital relationships (Review)

sama noor,[1,*] mina noor,[2]

1.
2.

Introduction: Infertility is considered one of the main genetic problems, and defined as impotence in pregnancy after one year of intercourse, without using any contraceptive method.According to past studies, about 50 to 80 million suffer this condition, while throughout the world one couple in six couples is afflicted with this condition.Impotency as a crisis is a source of social anxiety which overshadows all aspects of individual's life together with its physical, psychological and economic issues.Moreover, the couple's life expectations are challenged by being diagnosed with this condition, for infertility is an unplanned and unwanted anxiety factor, while many couples are not equipped with adequate knowledge and skill to cope with this issue.In a study titled "comparison of stress, depression and satisfaction Faal-Kalkhoran indicates that stress and depression exists in infertile couples and the main cause behind this is the people's attitude towards life management and social acceptance.This study sets out to investigate marital burnout and relationship beliefs among infertile and fertile couples in ardabil, Iran

Methods: The population of this descriptive-correlational study comprises of fertile and infertile couples seeking treatment from ardabil Infertility Treatment Clinic (2017). Via convenience sampling, 140 fertile and 140 infertile couples were selected according to medical criteria. The participants filled out the demographic data, Pine's Burnout Measure, and Epstein and Eidelson's Relationship Belief Inventory questionnaires. The data were analyzed through descriptive statistical methods, step by stem regression, one way variance analysis, Scheffe's tests, multi variable variance analysis, and independent T-test by SPSS version 18

Results: All the scores concerning relationship beliefs were higher in the fertile group in comparison to the scores within the infertile group, except for the destructiveness belief and inflexibility of the spouse (respectively P=0.27, P=0.24) other factors in the fertile and infertile groups were significantly different. Regarding the marital burnout factor, the scores pertaining to psychological burnout were significantly higher in the infertile group (P=0.0015). Although the scores pertaining to physical burnout were higher in the infertile group, and emotional burnout was higher in the fertile group, these differences were not significant.

Conclusion: Compared to the fertile group, the infertile couples are characterized by stronger relationship beliefs, but they experience higher marital burnout in physical and psychological dimensions

Keywords: Fertility, Marital burnout, Relationship beliefs

Evaluation of miR-551 and miR-6 as Diagnostic and Therapeutic Biomarkers for Gastric Cancer Associated with Helicobacter Pylori with Bioinformatics Approach (Research Paper)

Sara Fakharian Kashani,[1] Zainab Abedini,[2] Aynaz Farhang Darehshouri,[3] Kimia Jazi,[4] Hamid Taghvaei Javanshir,[5] Ahmad Bereimipour,[6,*]

1. Cancer Research Center, Tehran University of Medical Sciences, Tehran, Iran
2. Medical Genomics Research Center, Tehran Medical Sciences Islamic Azad University, Tehran, Iran
3. Medical Genomics Research Center, Tehran Medical Sciences Islamic Azad University, Tehran, Iran
4. Student research committee, faculty of medicine, medical university of Qom, Qom, Iran
5. Cancer Research Center, Tehran University of Medical Sciences, Tehran, Iran
6. Department of Stem Cells and Developmental Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran

Introduction: Gastric cancer is the 6th most prevalent cancer in the world (1). Although the worldwide mortality rates stand the 5th, gastric cancer rates 3rd and 1st in prevalence and mortality respectively among the Iranian population (1). Helicobacter pylori (HP) as a group 1 or definite carcinogen(2). HP releases urease, protease, phospholipase, ammonium, and acetaldehyde and thus disturbs the gastric mucosal barrier; moreover, it induces reactive oxygen production and suppresses the antioxidant defense mechanisms of the host, and result in oxidative damage (3). Furthermore, HP could cause gastric cancer by increasing endogenous DNA damage, reducing nuclear and mitochondrial mutation, and repairing DNA activity, resulting in aberrant DNA methylation (4). To reveal treatments and early-screening strategies, this study intended to evaluate the genes, functioning proteins, and related miRNAs through which HP provokes gastric cancer to track gene expression patterns, miRNA expression regulations, and active proteins and reveal potential therapy targets.

Methods: This investigation relied on bioinformatics analysis. Based on this, the GEO database was used to find the microarray gene expression profile. For this purpose, gastric cancer datasets GSE65801 without Helicobacter pylori and GSE116312 with Helicobacter pylori were chosen. The GEO 2 R analysis was then completed, followed by the Venn tool subscriptions. The signaling pathway was created using the Enrichr database, and molecular function and biological process data were found in the GO database. As a

result, the Hub genes were discovered using the STRING tool. The miRTarBase database was also used to identify miRNAs.

Results: The result of the analysis shows that 77 genes with high expression and 89 genes with low expression were classified as gastric cancer genes with helicobacter pylori infection. Negative regulation of interleukin-5 product, EGFR/EGF signaling pathway wp437, Activation of the Ap-1 family of transcription factors Homosapiens R-HAS-450341, and Negative regulation of activated T cell proliferation were observed in low expression genes. In the overexpressed gene, we observed protein serine/threonine kinase activator activity, Protein phosphatase activator activity, External encapsulating structure organization, and Regulation of T-helper 1 cell cytokine production as signaling pathways. EGFR, PTK2, EPHB2, HOXA7 proteins are significantly associated with downregulated genes, and CALR, Hist1H31, Hist1H3f, Hist1H4h, Hist1H2BB is related to upregulated genes. And among these proteins hsa- miR-551, hsa- miR-1, hsa- miR-6 were significantly associated with more genes.

Conclusion: In general, bioinformatics analysis can more accurately assess the relationship between gastric cancer with Helicobacter pylori infection. Selecting a panel of appropriate biomarkers present in the extracellular matrix and extracted through various human flows is the right solution for early detection, followed by proper treatment management and mortality reduction. This study focuses on EGFR, PTK2, EPHB2, HIST1H3F, HIS1H4H, proteins and hsa-miR-6, hsa- miR-551 miRNA released into the extracellular matrix provided various biomarkers for stages of gastric cancer, which require more extensive studies to investigate and find more precise mechanisms of these proteins.

Keywords: Biomarkers Discovery, Gastric Cancer, Bioinformatics Analysis, ECM, Helicobacter pylori

Evaluation of mutagenicity of Covid-19 virus and the effect of morphine in its treatment (Research Paper)

Ali Khanifar,[1,*]

1. Kurdistan university of medical sciences

Introduction: In this article, we will discuss the mutagenicity of Covid virus 19 and the effect of morphine in its treatment. Because the Covid 19 virus belongs to the corona virus family, which includes viruses with a single-stranded, positive-strand RNA genome. Of course, I have to point out that among the RNA viruses, those with the fragment genome have the highest mutagenicity, such as the influenza virus, which belongs to the orthomyxoviridae family, which contains the fragment RNA genome. However, the mutagenicity of Covid 19 virus is considered as an exception among RNA viruses that have a continuous genome. It is important to note that the Covid 19 virus can remain dormant between cells, where it fuses with the cell genome to produce a genome different from the genome that first entered the body, resulting in a mutation in the virus. Covid 19 treatment with morphine is inspired by the effect of morphine on the flu. The person with the flu, after a few hours of taking morphine, all the symptoms caused by the flu disappeared.

Methods: Because some viruses have the ability to hide in the host cell and resume their activity immediately after the weakening of the immune system. Like these viruses, the Covid 19 virus has the ability to hide in the host cell, and after combining with part of the host cell genome, mutations occur in the virus. It should be noted that this mutagenicity has manifested itself in people with weak immune systems and they do not necessarily have to travel to the rest of the world to catch it. Covid 19 is one of the best candidates for Covid 19 treatment because morphine eliminates most of the symptoms caused by morphine. By taking morphine, we find that it neutralizes at least 4 to 5 of the symptoms of Covid 19, including severe cough, severe pain, chronic diarrhea, and even stress if the person has Covid 19.

Results: This increases heart rate and respiration rate With morphine, not only do the three symptoms listed above go away, but there is also a relative calm that slows the heart rate and, most importantly, reduces the rate of respiration. Creates a competitive environment with the virus. In fact, the slower the rate of respiration and blood flow, the more immune cells can detect it. It should be noted that people who survive of Covid 19 have a higher level of relaxation because our immune system is able to detect the virus by reducing Blood flow velocity and people who are unable to do so are prescribed morphine will do this for them.

Conclusion: Because morphine has a high percentage of addiction, it should not be used more than twice. Also, in older people with weakened immunesystems, in addition to morphine, it should be taken from the serum of people rescued from Covid 19, which contains antibodies.

Keywords: Morphine-covid 19 - Mutation - Relaxation - Mixed

Evaluation Of Mycoflora Biodiversity Of In Indoor And Outdoor Tehran Airborne In 2018-2019, Iran (Research Paper)

Mohaddeseh Larypoor,[1,*] Ali Akhavan sepahy,[2]

1. Islamic Azad University, North Tehran Branch,Tehran, Iran
2.

Introduction: Introduction: Halotolerant fungi in the air produce a large number of industerial enzymes. Some of these fungi cause deadly opportunistic infections in humans. The purpose of this research is screening of fungi in the air of indoor and outdoor environments in Tehran

Methods: Methods: Air samplers, SAS Super DUO 360 were used for air sampling . 500 samples were taken from 44 sites in 11 geographical areas of Tehran during 2018 to 2019. The plates were incubated at 28° C for 2 to 4 weeks. The fungi colonies were purified and identified according to microscopic and genetic methods.

Results: The results: A total of 3596 colonies belonging to 15 fungal species were isolated. Of the city's central areas (8,9,10) 15 (25.33%) , northwestern region(5)9(12.60%), the northeastern region (4) 10 (15.7%), northern areas (3,2,1) 15 (24.24%) and southern areas (15,20, 22) 13 (22/02%)fungi were isolated. Airborne fungi have been identified in four groups: Hyaline saprophytes (63/75٪), dematiaceous saprophytes (33/69%), zygomycetes (8/50%) and Unidentifiable sterile mycelium (1.2%) . Aspergillus (31.31%), Cladosporium (21.30 %), Penicillium (17.15٪), Alternaria (11.32 %), Mucor (3.94%), Rhizopus (3.64٪), Fusarium (3.22%), Monilia (3/01%), Trichoderma (1.33%), Scopulariopsis (1.27%), Basidiobolus (0.92%), Chrysosporium (0.66%), Chaetomium (0.55%), Nigrospora (0.52%), Purpureocillium (0.30%) are identified genera and theirThe phylogenetic tree was also drawn.

Conclusion: Conclusion: The results show that outdoor air, can be a major source of pollution in indoor environments and providing a pattern for the spread of these fungi can help to reduce the risk of fatal opportunistic infections and allergic diseases.

Keywords: Airborne fungi, Outdoor air, Phaeohyphomycetes, Zygomycetes

Evaluation of PHB2 expression levels in breast cancer (Research Paper)

Zeynab Shaghaghi Torkdari,[1] Mohammad Khalaj-Kondori,[2,*] Mohammad Ali Hosseinpour Feizi,[3] Vahid Montazeri,[4]

1. University of Tabriz
2. University of Tabriz
3. University of Tabriz
4. University of Tabriz

Introduction: Breast cancer is the most important cause of cancer mortality among women that the study of its causative or aggravating factors seems necessary. In current study, the mRNA levels of PHB2 gene were evaluated in tumor and adjacent non-tumor tissues of 50 women diagnosed with invasive ductal carcinoma of breast.

Methods: RNX-Puls reagent was applied to isolate total RNA from tumor and adjacent non- tumor tissues of breast cancer patients. Thereafter, total RNA was converted to cDNA using Prime Script TM RT reagent kit. The mRNA levels of PHB2 were quantified by qRT-PCR and data was analyzed with paired sample t test. Furthermore, ROC curve analysis was performed to evaluate biomarker capacity of PHB2 in breast cancer tumor tissues.

Results: The significant low level of PHB2 mRNA was observed in tumor tissues of breast cancer patients compared with adjacent non-tumor tissues ($P<0.05$).

Conclusion: Low mRNA levels of PHB2 gene in breast cancer patients significantly discriminate the tumor from non-tumor tissues.

Keywords: Breast cancer, PHB2, Downregulation

Evaluation of preimplantation genetic diagnosis (Review)

Zahra Sadat Aghaei Shahri,[1,*]

1. Zahra Sadat Aghaei Shahri Member of the Research Committee of the Islamic Azad University of Mashhad. Iran

Introduction: Preimplantation Genetic Diagnosis (PGD) Cytogenetic analysis is performed to determine the presence or absence of genetic disease in the zygote before implantation. In vitro fertilization is an assisted reproductive technique. Chromosomal abnormalities are disorders of the number or structure of chromosomes. Genetic diseases Diseases caused by genetic mutations that may be inherited from the parents' genome or created in the womb.

Methods: Articles reviewed in databases published in 2002-2021 . Search by keywords Chromosomal abnormality, Preimplantation genetic diagnosis (PGD), Single gene disorder, In vitro fertilization .Eight articles from the google scholar database and 11 articles from the pubmed database were selected. 5 articles from the google scholar database and 5 articles from the pubmed database were removed due to non-compliance, and finally 9 articles were reviewed.

Results: in 1 article states that PGD was introduced in the early 1990s. in 9 article states that PGD is used to prevent the transmission of defective genes to the fetus and termination of pregnancy in couples who have chromosomal inherited disorders or a family history or have a child with a genetic disorder. In 3 articles, it is stated that in PGD, single-gene abnormalities, hereditary chromosomal abnormalities and X-related abnormalities are detected in the fetus before entering the uterus, and with consent and by considering the usual criteria in an appropriate time frame, prevention of Continuation of pregnancy is done. Based on 7 studies, In PGD, 18-16 hours after fertilization, the ovums are evaluated for fertilization and those that have suitable characteristics are cultured. Then, on the third day, when the embryo is in the 6- to 8-cell stage, one or two blastomeres are isolated and the cell's DNA is amplified. They are evaluated for genetic diseases, and if they are healthy, the embryo is transferred to the mother's uterus. But in case of infection, the transfer does not take place. In this method, instead of trying to get pregnant several times, more embryos are formed during an IVF period and the embryos are genetically examined. They are more likely to have a healthy fetus. Termination of pregnancy and recurrent miscarriage no longer occur. In one study, the use of PGD to diagnose the risk of late-onset diseases and cancer-prone genes was also discussed. An article on the disadvantages of PGD states that there are a number of misdiagnosis cases and they are very expensive.

Conclusion: People with special hereditary conditions should be under the care of an embryologist, gynecologist and geneticist and with careful counseling and awareness of the limitations and costs, they can use the PGD method to prevent the transmission of defective genes to their offspring and reduce the risk of miscarriage.

Keywords: Chromosomal abnormality, Preimplantation genetic diagnosis (PGD), Single gene disorder, In vitro fer

Evaluation of resistance gene in Shigella sonnei to Azithromycin treatment: A Systematic Review (Review)

Fatemeh Alvani,[1,*] Babak Elyasi Far,[2] Hamideh Alvani,[3]

1. Mehregan 2 School Of Abadan
2. Education Department Of Shushtar
3. Education Department Of Abadan

Introduction: Introduction: Shigellosis is an intestinal infection caused by Shigella bacteria. Globally, shigellosis occurs in at least 80 million people and kills about 700,000 people annually. In severe cases, antibiotics may be used, but resistance is common. Ciprofloxacin and azithromycin are commonly used to treatment of the disease.

Methods: Method: A Systematic Review of the current published literature on Shigella sonnei resistance gene to azithromycin was performed according to the preferred report items for systematic review.

Results: Results: Azithromycin is one type of acid stable orally administered macrolide used to treat a number of bacterial infections. Azithromycin is increasingly used to treat shigellosis despite the lack of interpretive guidelines and limited clinical evidence. The present study determined the susceptibility of azithromycin and linked it to macrolide-resistant genes in Shigella spp. Our study shows that DSA was severe for Shigella sonnei isolates and that the mphA gene was collected by plasmid, the most common macrolide resistance gene detected in Shigella isolates.

Conclusion: Conclusion: Monitoring of Shigella susceptibility and studying the mechanism of Shigella resistance to azithromycin, due to the limited choice of treatment for shigellosis, are essential. The azithromycin treatment failures demonstrate the importance of clinical points in assisting physicians in identifying alternative treatment options for resistant strains. In addition, these therapeutic failures highlight the need for comprehensive sensitivity testing and systematic results, especially given the emergence of drug-resistant Shigella among a wide range of patient populations.

Keywords: Keywords: Shigella sonnei, Azithromycin, Drug resistance, Resistance gene

Evaluation of SARS-CoV-2 shedding in the upper respiratory as well as blood, stool, and urine specimens of infected patients (Research Paper)

Mahdieh Mondanizadeh ,[1] Behzad Khansarinejad,[2,*]

1. Department of Biotechnology and Molecular Medicine, Arak University of Medical Sciences, Arak, Iran
2. Department of Microbiology and Immunology, Arak University of Medical Sciences, Arak, Iran

Introduction: Coronavirus disease 2019 (COVID-19) is an infectious disease caused by a newly discovered coronavirus. Understanding the spreading routes of SARS-CoV-2 is crucial for patient management and defining biosafety strategies for public and health care workers. in the current study, the virus shedding in the upper respiratory as well as blood, stool, and urine specimens of infected patients, was examined using quantitative real-time PCR assay (qRT-PCR).

Methods: The samples of 50 positive patients with high, moderate, and low virus titers in their respiratory specimens were collected. All specimens were subjected to RNA extraction and RT-qPCR assay using two different internally-controlled test systems.

Results: The results indicated that no positive results were observed in the urine samples of all patients. The viral genome was diagnosed in 5% of blood and 3.3% of rectal swab samples. The Cq (Cycle of quantification)-values of positive results on the stool and blood samples were always higher than the Cq-value of the respiratory specimen of the same patient.

Conclusion: SARS-CoV-2 is mainly detected in the respiratory samples, and the virus is not detectable in the urine. The importance of viremia and the existence of the virus in feces in virus spread in the human population needs further investigation.

Keywords: Coronavirus , COVID-19 , SARS-CoV-2, RT-qPCR

Evaluation of SCAMP5 gene expression in the tissues of Iranian patients with glioblastoma multiforme (Research Paper)

nasrin Karimi,[1] Hamidreza Kheiri Manjilli,[2,*] Vajiheh Zarrinpour,[3] Mohammadmehdi Forghanifard,[4]

1. Department of Biology, Faculty of Basic Sciences, Islamic Azad University, Damghan Branch, Damghan, Iran
2.
3. Department of Biology, Faculty of Basic Sciences, Islamic Azad University, Damghan Branch, Damghan, Iran
4. Department of Biology, Faculty of Basic Sciences, Islamic Azad University, Damghan Branch, Damghan, Iran

Introduction: Glioblastoma multiforme (also called glioblastoma, GBM) is uncommon cancer that accounts for more than half of the primary malignant brain tumors diagnosed. The study of the expression of genes involved in glioblastoma can be effective in early detection, so we discussed the clinical significance and biological role of the SCAMP5 gene transcript in glioblastoma cancer, which is unknown.

Methods: In the present study, 25 samples of healthy tissue margin of glioblastoma multiform were used as a control group and 25 samples of glioblastoma multiforme tissue as a patient group were obtained before treatment and RNA extraction and cDNA synthesis were performed. SCAMP5 expression levels were assessed by Real time-PCR. ACTB was used as the internal control. Statistical analysis was performed by GraphPad Prism v.8.0.1.

Results: Down-expression of SCAMP5($P<0.05$) in glioblastoma multiforme tissue samples was significant compared to healthy tumor margin tissue. Expression of SCAMP5 gene with age with P-value = 0.0024 is statistically significant. But the expression of this gene with gender with P-value = 0.4611 is not statistically significant. Decreased expression of the SCAMP5 gene can play an important role in glioblastoma cancer.

Conclusion: SCAMP5 was expressed in tumor tissue of patients with GBM lower than healthy tissue around the tumor. According to this study, it may be possible to use the expression of this gene as a marker as an early diagnostic method, but needs further study.

Keywords: Glioblastoma multiforme, SCAMP5, Real time-PCR, expression

Evaluation of sexual function and sexual quality of life in men with genital warts (Research Paper)

Roksana Janghorban,[1,*] Marzieh Hosseininia,[2]

1. Department of Midwifery, School of Nursing and Midwifery, Community Based Psychiatric Care Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
2. Department of Midwifery, School of Nursing and Midwifery, Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran

Introduction: Background: Human papillomavirus is the most common sexually transmitted infection, which usually occurs after the first sexual activity and may affect men's sexual health. The present study was performed to evaluate sexual function and sexual quality of life of men with genital warts.

Methods: Methods: This cross-sectional study was conducted from September to March 2019 with a sample size of 105 men in the dermatology clinic of Shahid Dr. Faghihi Hospital in Shiraz University of Medical Sciences. Data were collected by demographic questionnaire, the International Index of Erectile Function (IIEF) and men sexual quality of life questionnaires and were analyzed using descriptive and inferential tests with SPSS software version 22.

Results: Results: The mean of overall sexual function score in men was 48.50 ± 8.89. 35.2% of men had general sexual dysfunction. The highest rate of disorder was related to the erection domain (85.7%) and the lowest rate was related to the desire domain (5.7%). In the erection domain, most men (54.3%) had experienced mild to moderate erectile dysfunction. The mean total score of men's sexual quality of life was 38.36 ± 14.47 And 56.2% of them had a good sexual quality of life.

Conclusion: Conclusion: Genital warts could be affected men's sexual function and sexual quality of life. Therefore, the appropriate program is necessary to promote men's sexual health in this group.

Keywords: Sexual Function, Sexual Quality of life, Human Papilloma Virus, Genital warts

Evaluation of sexual function and sexual quality of life in women with genital warts (Research Paper)

Roksana Janghorban,[1,*] Marzieh Hosseininia,[2]

1. Department of Midwifery, School of Nursing and Midwifery, Maternal-Fetal Medicine Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
2. Department of Midwifery, School of Nursing and Midwifery, Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran

Introduction: Introduction: Human papillomavirus is the most sexually transmitted infection that usually occurs after the first sexual activity. Infection with this virus and the occurrence of genital warts have many physical, psychological and social consequences on patients. Because the sexual response cycle is a reflection of the interactions between bio-psychological and social factors and the quality of sexual life is largely affected by sexual function therefore, we decided to design this study with the aim of evaluating the performance and quality of sexual life of women with genital warts.

Methods: Methods: This study is a cross-sectional study that was performed on 105 females with genital warts referred to the dermatology clinic of Shahed Faghehi Hospital of Shiraz University of Medical Sciences in 2019. Demographic information were collected by a researcher-made questionnaire. Then, the female sexual function index questionnaire and the female sexual quality of life questionnaire were completed by female samples. Data were analyzed by SPSS software version 22.

Results: Results: The mean score of female sexual function index was 19.03 ± 3.82 and 97.1% of women with genital warts reported general sexual dysfunction and the severity of the disorder was mild. The mean total score of sexual quality of life in women was 52.29 ± 20.63 and 66.7% of women had moderate sexual quality of life.

Conclusion: Conclusion: The results of the study showed that a high percentage of women with genital warts had general sexual dysfunction, but the severity of this disorder was mild in women. However, the same mild severity of female sexual dysfunction had a greater impact on their quality of sexual life and a higher percentage of women experienced moderate quality of sexual life.

Keywords: Keywords: Sexual function, sexual quality of life, human papillomavirus, genital warts

Evaluation of sexual health of infertile women (Review)

Mohammad amin Masoumi,[1,*] zeinab sadat moosavifard,[2]

1. BSc in Nursing, Department of Nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.
2. Department of Nursing, Faculty of nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.

Introduction: According to the definition of the World Infertility Organization, failure to achieve clinical pregnancy following 12 months of unprotected sex is defined. Infertility is one of the most common diseases of women that is associated with problems in the physical, mental and social spheres. Endanger health One of the dimensions of health is sexual health. Therefore, the present study was conducted to determine the sexual health of destroyed women.

Methods: The following study is a review study of the search sites and databases, SID Google scholar, Scopus, Iran medex, pubmed, Magiran, Elmnet, with the keywords sexual health, infertility, women's health, problems Sex, reproductive health, risk factor and their English equivalent were performed without time interval. Of all the articles found, 15 were descriptive B-analytical articles in accordance with the purpose of the study, which were entered into the review cycle and used.

Results: According to the evidence in most studies, infertile women had poor sexual health. In general, infertility has a negative effect on the quality of family planning, sexually transmitted diseases such as AIDS and cervical cancer, sexual satisfaction, violence against women, gender-based violence and high-risk sexual behaviors. They disrupt, so that infertility has the greatest impact on violence against women and the least impact on high-risk sexual behaviors.

Conclusion: According to the results of studies, infertility affects various aspects of sexual health. On the other hand, due to the fact that sexual health is the guarantor of the health of the family center and its importance is such that sexual health disorders are directly related to family family disorders. Health, especially in infertile women, and by holding training classes to help promote women's sexual health, as well as health professionals and those interested in conducting more research on sexual health.

Keywords: Infertility, sexual health, women

Evaluation of stress, anxiety and depression during pregnancy and its related factors during the COVID-19 Pandemic (Review)

Zahra Zare ,[1,*] Mojtaba Laal Ahangar,[2]

1. Department of Midwifery, Faculty of Nursing and Midwifery, Sabzevar University of Medical Sciences, Sabzevar, Iran.
2. Msc of Nursing, Sabzevar University of Medical Sciences, Sabzevar , Iran

Introduction: Introduction: Covid 19 pandemic has many effects on people's mental health and has led to high levels of depression and anxiety. Pregnancy is a period of elevated risk for mental health difficulties, which are likely exacerbated during the COVID-19 pandemic. The aim of this study is to investigate stress, anxiety and depression during pregnancy and its related factors during the COVID-19 Pandemic.

Methods: Methods: This review study articles on the related topic were searched in the following databases; Google scholar, SID, Magiran , Iranmedex , Scopus, Web of Science, PubMed, Science direct. A total of 26 related research papers, between 2019–2021 were included in this study.

Results: Results: The result of the study showed prevalence of COVID-19 has a negative effect on the mental health in pregnant women. Stress, anxiety and depression increased in pregnant women during COVID-19 pandemic. Factors such as perceived social support from family and spouse, participation in health behaviors, positive self-assessment of pregnancy and higher education level have a protective role against psychological problems during pregnancy. On the other hand, factors such as lower age, lower income, fewer children, unemployment, high-risk pregnancies, lower gestational age increase the risk of anxiety, stress and depression in pregnancy

Conclusion: Conclusion: The incidence of anxiety, stress and depression in pregnant women was high during the COVID-19 pandemic. In critical situations, such as recent pandemic; appropriate prevention, early interventions and access to mental health services are essential to prevent of dysfunction and preserve the mental health in pregnant women.

Keywords: COVID-19, pregnancy, depression, stress, anxiety, mental health

Evaluation of the antibacterial activity of some medicinal plants on Listeria monocytogenes (Review)

Yousef Alaee Mollabashi,[1,*] Peyman sefidi,[2] Nima Foroutan,[3]

1. Department of Biology, Tabriz Branch, Islamic Azad University, Tabriz, Iran
2. Department of Biology, Tabriz Branch, Islamic Azad University, Tabriz, Iran
3. Department of Biology, Ardanil Branch, Islamic Azad University, Ardabil, Iran

Introduction: One of the gram-positive bacteria that is highly important in terms of pathogenicity in food sources used by humans and in recent years studies have been conducted to investigate the prevalence of this bacterium and controls to reduce its activity is the rod-shaped bacterium Listeria monocytogenes. This catalase-positive, spore-free bacterium can have profound and severe effects on infants and the elderly, such as death, which is more common than in people of other ages. Listeria monocytogenes bacteria, when it enters a person's body, we see various complications and diseases such as meningitis, abortion in pregnant women, etc. In most cases, human listeriosis is caused by Listeria monocytogenes serotype 4. Among the factors that have been proven in various studies and can increase the risk of pathogenicity of this bacterium, the presence of this bacterium in different environments and foods and even low storage temperature is not a barrier against the activity of this oxidase-negative bacterium and sodium chloride also, up to 10 to 12.5% is not effective on the activity and proliferation of this bacterium. Other risk factors include the very small amount of this bacterium that can cause infection in the host. On the other hand, in 2008 it was stated that about 70% of infectious diseases are transmitted through food. In the case of Listeria monocytogenes, it can be said that various foods from vegetables to dairy, from seafood to other food sources can be contaminated and transmitted, but raw milk and soft cheese are the most contaminated in dairy products with Listeria monocytogenes. Now, chemical or natural preservatives can be used against the activity of this pathogenic bacterium, but because some people in the community think that preservatives are of chemical origin, pay attention to natural and plant preservatives such as plant extracts and essential oils that can eliminate pathogens are attracted. Essential oils are obtained in liquid and fragrant form from the plant. The vulnerability of the cell wall of microbial pathogens against essential oils derived from medicinal plants is one of the causes of microbial death. In the essential oils of medicinal plants, there are many compounds such as alpha-pinene, gamma-terpinene, phenol, etc that play an important role. In addition to bacteria, plant essential oils can also be used to kill molds and yeasts. During the many years that essential oils have been used as a preservative, not only promising results have been observed, but also the effect on the taste, smell, colour, etc. of the food has prevented the essential oils from

being widely used. The purpose of this review article is to review the results of a series of studies on the anti-listerial properties of some medicinal plants.

Methods: Using keywords related to the purpose of this study, such as the antibacterial properties of medicinal plants, anti-listerial activity of medicinal plants, etc., we applied to find the desired references without applying a specific time interval.

Results: In a study conducted by Dr Jalali et al., the hydroalcoholic extract of eucalyptus showed more and better anti-listerial effects in both tubular dilution and disc diffusion methods than the other plants studied in that study. The result of a study in 2008, in which mint oil extract was inoculated at three different concentrations on 1000000 Listeria monocytogenes bacteria was used per gram of cheese at two different temperatures of 7 and 15 ° C at regular intervals. And they reported that mint extract was effective against this gram-positive bacterium. In previous years, black seed was used on the growth and activity of this bacterium, and in addition, the antibiotic gentamicin was used, which was reported to be much more effective than the antibiotic used. In one study, researchers used 3 concentrations of thyme extract on Listeria monocytogenes, and at the end of that study, the antimicrobial effect of this plant extract was confirmed. Comparing the results of different studies for various reasons such as essential oil production, plant growth stages, low concentration of essential oil in the extract, type of solvent, extraction method, etc. is more difficult to easily comment on the effectiveness of different plants.

Conclusion: Nowadays, due to various problems in controlling and suppressing pathogens by a group of common drugs and the need of the international community to develop new and effective therapies such as medicinal plants with antimicrobial properties, nanoparticles, etc is needed.

Keywords: Antibacterial, Medicinal plants, Listeria monocytogenes

Evaluation of the Antimicrobial Effect of Montain Savory and Purple Coneflower Extracts on Staphylococcus aureus in vitro and Animal Model Study (Research Paper)

Nader Kazemi,[1,*] Kosar Abolfazli Zanjani,[2]

1. 1 Department of Biology, Nanobiotechnology Research Center, Zanjan Branch, Islamic Azad University, Zanjan, Iran
2. 2 Department of Microbiology, Nanobiotechnology Research Center, Zanjan Branch, Islamic Azad University, Zanjan, Iran

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.

Methods: In this study, aqueous and ethanolic extracts were prepared from dried leaves of the Satureja montana and Echinacea angustifolia, 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 Satureja montana (20 mm), and the minimum of growth inhibition diameter is related to ethanolic extract of Echinacea angustifolia (10 mm) at the highest concentration (400 mg/ml). In conditions of in vivo, after 48 hours spleen supernatant cultivation, the average number of bacteria for ethanolic extracts of the Satureja montana and Echinacea angustifolia were 1.8×103 CFU/ml and 6.6×103 CFU/ml respectively and for aqueous extract of Satureja montana 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 Satureja

montana and ethanolic extract of Echinacea angustifolia have the effective antibacterial activity against mentioned bacteria and can be useful to treatment of nosocomial infections.

Keywords: Antimicrobial, Echinacea angustifolia, Satureja montana, Staphylococcus aureus

Evaluation of the effect of black garlic in reducing heart disease (Review)

Mohamad mehdi Morshedi,[1,*]

1.

Introduction: Garlic has been used as a medicinal plant since ancient times and is less used because of its unpleasant odor, but it can be converted raw garlic into black garlic by certain methods, which has a far higher nutritional value than garlic and can be useful in the treatment of many patients.

Methods: Black garlic is made from raw garlic under temperatures (60 to 90 °C) and controlled moisture (70-90%) over the period of 40 to 90 days and their minerals are measured during the specified days.

Results: According to studies and experiments conducted from black garlic, the amount of antioxidants, polyphenols and flavonoids increases and the amount of sugars in it decreases during the thermal process and also the pH of garlic becomes more acidic.

Conclusion: Garlic and its products are widely known around the world for the prevention of heart disease, and black garlic is very useful due to its high antioxidants.

Keywords: Black garlic - heart disease

Evaluation of the effect of conditioned media of mesenchymal stem cells treated with ascorbic acid on viability and proliferative behavior of breast cancer cell (Research Paper)

Fattane Sam Daliri,[1] Narges Toolabi ,[2] Mahmood Talkhabi,[3,*] Farnoosh Attari,[4] Mousa Kehtari,[5]

1. Department of Animal Sciences and Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
2. Department of Animal Sciences and Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
3. Department of Animal Sciences and Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
4. Department of Animal Biology, School of Biology, College of Science, University of Tehran, Tehran, Iran
5. Department of Stem Cell Biology, Stem Cell Technology Research Center, Tehran, Iran

Introduction: Breast cancer is one of the most common types of cancer in women. This cancer is a complex of specific malignancies in the mammary glands. Mental problems caused by surgeries, as well as death due to the spread of the disease, are factors that endanger women's health. Nowadays researchers are looking for new method of cancer treatment. The use of stem cells is one of the applied approaches in field of cancer. Among the types of stem cell, mesenchymal stem cells due to their ability to interact with the microenvironments of cancer cells are consider as an appropriate option. conditioned media of mesenchymal stem cells and their secretive factors affect cancer cells. However, the results of application of these cells in the treatment of cancer is controversial. One of the challenges in using stem cells is the limitations on the proliferation and differentiation Potential of these cells for clinical applications. One of the factors affecting stem cells is ascorbic acid. Ascorbic acid is an effective antioxidant on the proliferation and differentiation of mesenchymal stem cells, which also affects the function of cancer cells.

Methods: In this study, investigated the effect of conditioned media of human Adipose-derived Mesenchymal Stem Cells treated with ascorbic acid on proliferative behavior of breast cancer cells. Initially, human Adipose-derived mesenchymal stem cells were constructed from the stem cell center in the first passage, and breast cancer cells (cell line 4T1) in the fifth passage were prepared from the University of Tehran and cultured for use. In order to obtain the desired concentration of ascorbic acid, by reviewing the articles and performing MTT test for 4T1 cells, considering the cell viability above 50% of 4T1 cells, a concentration of 1 mM was selected. Ascorbic acid was treated to mesenchymal cells at a concentration of 1 mM and the resulting conditioned

media was collected. The obtained conditioned media was added to 4T1 cells in different groups. In this study, 4 groups were considered and 4T1 cells were treated with these groups for 24 hours and examined. Groups included 4T1 cells treated with conditioned media of mesenchymal stem cells without FBS, without ascorbic acid, the second group, 4T1 cells treated with conditioned media without FBS, contains ascorbic acid with a concentration of 1 mM, the third group, 4T1 cells treated with conditioned media containing 5% FBS, ascorbic acid free and in the fourth group, 4T1 cells treated with conditioned media containing 5% FBS and 1 mM ascorbic acid were determined. Evaluations included cell morphology, apoptosis and cell cycle by Flow cytometry technique.

Results: The results of the effect of conditioned media of mesenchymal stem cells on the morphology of 4T1 cells showed that in groups with ascorbic acid, there were more changes in cells morphology and cell proliferation was reduced. In studies performed by flow cytometry, apoptosis and cell cycle were evaluated. According to the results of 4T1 cell apoptosis, the highest percentage of cells in the apoptotic stage belonged to the group without FBS and had ascorbic acid. Cell cycle analysis showed that, the group in which 4T1 cells were treated with FBS conditioned media and without ascorbic acid, formed the highest percentage of S-phase cells in the cell cycle.

Conclusion: The results of the study showed that the conditioned media of mesenchymal stem cells treated with ascorbic acid, reduces the proliferation of breast cancer cells, therefore, can be effective in controlling breast cancer.

Keywords: Breast cancer, Conditioned Media, Adipose-derived mesenchymal stem cell, Ascorbic acid, Cell prolife

Evaluation of the effect of Dichloroacetate-treated mesenchymal stem cell conditioned media on viability and proliferative behavior of breast cancer cells (Research Paper)

Narges Toolabi,[1] Fattane Sam Daliri,[2] Mahmood Talkhabi,[3,*] Farnoosh Attari,[4] Leila taghiyar,[5]

1. Department of Animal Sciences and Marine Biology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
2. Department of Animal Sciences and Marine Biology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
3. Department of Animal Sciences and Marine Biology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
4. Department of Animal Biology, School of Biology, College of Science, University of Tehran, Tehran, Iran
5. Department of Stem Cells and Developmental Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran

Introduction: Cancer is a disease caused by the overgrowth of malignant cells that can spread to other parts of the body. The development of breast cancer is a multi-stage process that begins in the cells of the breast and can be transmitted to distant organs. Drugs that affect cancer metabolism have been studied in recent decades. Many cancer drugs and cancer drug compounds have individual side effects. Dichloroacetate (DCA) has been studied as a new metabolic treatment for various cancers. The effects of stem cells or the conditioned media produced by these cells in the treatment or control of some cancers and tissue repair have already been demonstrated. This study investigates the effect of conditioned media of DCA-treated mesenchymal stem cells on the proliferative behavior of breast cancer cells based on cellular and morphological studies.

Methods: In this study, human adipose-derived mesenchymal stem cells were first prepared in passage 1 and propagated in the laboratory. Then, in passage 3, different doses of DCA were treated and after 24 hours, the viability rate was assessed by MTT assay. Also, 4T1 cell line was prepared in Passage 5 from the University of Tehran. Then, 4T1 cell line in passage 10, different doses of DCA were treated and after 24 hours, the viability rate was assessed by MTT assay. Then a dose of 1 mM was selected to collect the conditioned media. To prepare the conditioned media of human adipose-derived mesenchymal stem cells in passage three with four groups included: group without FBS and without DCA, group without FBS and with 1 mM DCA, group with 5% FBS and without DCA and group with 5% FBS and treated with DCA 1 mM and after 24 hours of conditioned media was collected for further experiments. Then 4T1 cells in 10 passages were treated with concentrations

100% conditioned media of 4 groups. Evaluations cell morphology, apoptosis and cell cycle by Flow cytometry technique were performed.

Results: Study of cell cycle and apoptosis on 4T1 cells treated with 100% conditioned media of group without FBS and with DCA compared to group without DCA, are able to induce S-phase cell cycle and induce apoptosis 4T1 cells. Comparison of the group with 5% FBS and with DCA compared to the group without DCA is able to induce S-phase cell cycle and inhibit apoptosis 4T1 cells. The results of the effect of conditioned media of mesenchymal stem cells on the morphology of 4T1 cells showed that in groups with DCA 1 mM, there were more changes in cells morphology and cell proliferation was increased.

Conclusion: The results showed that the conditioned media treated with low doses of DCA causes proliferation and cessation of apoptosis of 4T1 breast cancer cells.

Keywords: Breast cancer, Conditioned media, Adipose-derived mesenchymal stem cells, Dichloroacetate, Morpholog

Evaluation of the effect of probiotics in the prevention and treatment of gastrointestinal diseases (Review)

Mohammad Javad Forouzani-Moghaddam,[1,*]

1. Msc of Food Microbiology, School of Paramedical, Iran University of Medical Sciences, Tehran, Iran

Introduction: Probiotics are living microorganisms that have beneficial effects on gastrointestinal health. Probiotics do this by modulating the gut microbial flora. The aim of this study was to review the available clinical evidence on the effects of probiotics in the prevention and treatment of gastrointestinal diseases during the years 1995-2020.

Methods: Articles related to the subject were searched in PubMed and Science direct websites and clinical trials and systematic review articles examining the effects of probiotics in the prevention and treatment of gastrointestinal diseases were included in the study.

Results: There is currently good evidence for the therapeutic effects of probiotics on infectious diarrhea, antibiotic-induced diarrhea and lactose intolerance. Evidence has also been found on the beneficial effects of probiotics in the treatment of inflammatory bowel disease, irritable bowel syndrome, constipation, Helicobacter pylori infection, and the prevention of colon cancer. Different probiotic bacteria it is difficult to make a definite statement about the results of these studies. Further clinical studies are necessary to determine the effective dose and dose of probiotics in various diseases.

Conclusion: Probiotics can be used as adjunctive therapy in gastrointestinal diseases, but the need for further studies and appropriate design to clarify the efficacy and safety of probiotics in the prevention and treatment of gastrointestinal diseases and their mechanism of action.

Keywords: probiotics, ,prevention, treatment, gastrointestinal diseases

Evaluation of the effects of Extrecorpeal photophoresis (ECP) in the treatment of graft versus host disease (GVHD): A review study (Review)

nazi dezvaree,[1,*]

1. sgahid beheshti university

Introduction: Background and purpose: Exteracorpeal photophoresis (ECP) is an immunomodulatory therapy used to treat graft-versus-host disease (GVHD) Used in adults and children. Few studies have examined its use in children. The aim of this review study was to evaluate the effects of photophoresis in reducing the symptoms of GVHD in children.

Methods: Methods: This review article is the result of reviewing and studying various databases Med line, Pub Med, Scholar, Science Direct.

Results: Discussion: Host versus host disease is a common complication after hematopoietic stem cell transplantation (HSCT); As a result of the transplantation of immune cells from the donor, the patient's cells are identified externally. Thus, transplanted immune cells attack cells. The main affected organs are the skin, liver, and intestines, among other organ tissues. First-line treatment usually includes corticosteroids and in combination with other immunosuppressive agents in resistant cases. The limited effectiveness and severe side effects of these immunosuppressive drugs have led to the use of several alternative methods. photophoresis is an immune-modifying treatment that involves collecting immune cells from peripheral blood outside the body. These immune cells are then exposed to a photoactive agent (eg 8, methoxypsoralen) and subsequent UV-A radiation and then re-injected. The immunomodulatory effects of this method are not fully understood. Several current clinical studies recommend that photophoresis be considered in pediatric patients with acute and chronic graft-versus-host disease after hematopoietic stem cell transplantation.

Conclusion: Conclusion: In general, photophoresis is well tolerated in children and few side effects have been reported. As a result, photophoresis is a very safe treatment for GVHD in children with high clinical response rates, mainly in the skin and mucous membranes, and this reduces the dose of corticosteroids and other adjuvant immunosuppressants. Based on these observations and considering the multiple adverse effects of drugs used in this disease, it is concluded that in children with acute or chronic GVHD, photophoresis may be useful in reducing complications and mortality and improving quality of life.

Keywords: Keywords: Extrecorporeal photophoresis, graft versus host disease, children

Evaluation of the effects of Hypericum perforatum extract on HIV, IAV, and SARS-CoV-2 (Review)

Elham Aryanpour,[1] Atiyeh Abdolnuri,[2] Hadi Mohebalian,[3,*]

1. Department of Biology, Faculty of Sciences, Ferdowsi University
2. Department of Biology, Faculty of Sciences, Ferdowsi University
3. Department of Immunology and Virology, Faculty of Veterinary, Ferdowsi University

Introduction: Hypericum perforatum L. (St. John's wort) is a member of Hypericaceae family and an herbaceous perennial plant native to North Africa, Western Europe, Asia, and North America. This pharmaceutical plant has many features such as antidepressant, antitumor, antiviral and anti-inflammation. The antiviral and anti-inflammatory effects of this plant depend on the presence of two active ingredients; hypericin and hyperforin. In this review, we provide a broad overview of recent advances in the extraordinary effects of the Hypericum perforatum extract (consist of hypericin and hyperforin) on HIV, IAV, and SARS-CoV-2.

Methods: For this review article, all information was obtained in the English, German, Persian, French languages from search engines including Google Scholar, PubMed, Science Direct, Research Gate, and Embase. We used published articles until December 2020.

Results: Based on research, the antiviral effects of this plant are related to hypericin. Nonetheless, hypericin can only inactivate the viruses endowed with coats. A certain concentration of hypericin could inactivate HIV-1 in vitro and in vivo. hypericin interferes with the processing of the HIV Gag polyprotein (p55) and HIV p24 (main capsid protein). This function causes the production of immature or abnormally assembled cores, therefore; the virus is not able to encode viral antigens in infected cells and lost its infectivity. Some studies reported that hypericin by binding to main regions of SARS-CoV-2 can prevent virus assembly and infection. In IAV-infected mice, Hypericum perforatum extract can decrease the lung index and the secretions of TNF-α and IL-6 in serum and lung tissue. According to the new research, hyperforin is the main component that has anti-inflammatory effects and regulates immune system function. hyperforin prevent further cytokine production such as IL-1β, TNF-α, IL-6 and chemokines through the simultaneous inhibition of JAK/STAT (the Janus kinase/signal transducer and activator of transcription), MAPK (mitogen-activated protein kinases), NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells) pathways. Therefore, these mechanisms can limit the effects of the cytokine storm and prohibit severe local and systemic inflammation.

Conclusion: In some virus diseases, excess release of pro-inflammatory cytokines, imbalance in the regulatory mechanisms of the immune system, and spreading of viral infection cause exacerbation of the disease and even death. For instance, in COVID-19 patients, cytokine storm plays a major role in the death. We believe hyperforin through the inhibition of three main signaling pathways (JAK/STAT, MAPK, NF-κB) and hypericin due to its antiviral effects against coated viruses may be able to inhibit this kind of disease. In our opinion, Hypericum perforatum extract (consist of hypericin and hyperforin) can be used as a suggested option for the treatment. Although; this suggestion requires further research and clinical trials.

Keywords: Hypericum perforatum, cytokine storm, SARS-CoV-2, HIV, IAV

Evaluation of the efficiency of insulin-producing cells resulting from adipose tissue mesenchymal stem cell differentiation in glucose sensing and glucose stimulated insulin secretion (Research Paper)

Dian Dayer,[1,*] Elham Ghalami negad,[2] Seyed Javad Hosseini,[3]

1. Cellular and Molecular Research Center, Medical Basic Sciences Research Institute, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
2. Cellular and Molecular Research Center, Medical Basic Sciences Research Institute, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
3. Institute of Persian Gulf Research and Studies Center , Persian Gulf University (PGU), Bousher, I.R.IRAN

Introduction: Since insulin-producing cells resulting from stem cell differentiation cannot be as effective as pancreatic beta cells in regulating insulin-dependent glucose secretion, it seems necessary to identify the factors influencing this process. Therefore, this study was performed to investigate the changes in the expression of Glut2, ENO1, IGF-IR, Glucagon by insulin-producing cells resulting from the differentiation of adipose-derived mesenchymal stem cells.

Methods: Adipose-derived mesenchymal stem cells were differentiated into insulin-producing cells in a 14-day protocol using nicotinamide and ITS. The ability to produce insulin was confirmed by DTZ staining. Insulin and glucagon concentrations were determined by ELISA and the expression of Glut2, ENO1 and IGF-IR genes were measured by real time PCR.

Results: DTZ staining confirmed the presence of insulin secreting granules in insulin-producing cells. Differentiated cells secreted significantly more insulin and glucagon compared to undifferentiated cells. The differentiated cells showed significantly higher amounts of Glut2 and IGF-IR gene expressions compared with undifferentiated cells. While the expression of ENO1 was not significantly different between two groups.

Conclusion: The obtained insulin-producing cells exhibit the ability to naturally absorb glucose, perform glycolysis, and glucose-dependent insulin secretion in vitro.

Keywords: Insulin producing cells, Adipose tissue mesenchymal stem cells, Glut2, ENO1, IGF-IR, Glucagon

Evaluation of the expression of hsa_circ_0006990 in renal cell carcinoma and its relationship with clinicopathological information (Research Paper)

Zahra Firoozi,[1] Elham Mohammadisoleimani,[2] Mohammad Mehdi Naghizadeh ,[3] Ali Ariafar ,[4] Yaser Mansoori ,[5,*]

1. Department of Medical Genetics, Fasa University of Medical Sciences, Fasa, Iran.
2. Department of Medical Biotechnology, Fasa University of Medical Sciences, Fasa, Iran
3. Noncommunicable Diseases Research Center, Fasa University of Medical Sciences, Fasa, Iran.
4. Urology oncology research center, Shiraz University of medical sciences, Shiraz, Iran
5. Department of Medical Genetics, Fasa University of Medical Sciences, Fasa, Iran.

Introduction: Renal cell carcinoma (RCC) is one of the aggressive and highly metastatic type of kidney cancer. Although dysregulation of different genes in RCC development have been reported, the particular molecular mechanism is still unknown. Circular RNAs (circRNAs), a novel class of non-coding RNAs (ncRNAs), are involved in various biological processes in different cancers including RCC. The purpose of this study is to determine the expression of hsa_circ_0006990 in our RCC patients' tumors and adjacent normal tissues, as well as its association with clinicopathological features.

Methods: RNA extraction was done using TRIzol reagent (Invitrogen, USA). According to the manufacturer's protocol (Fermentas, Cat.No: K1622), the synthesis of cDNA (complementary DNA) was performed and after that, the hsa_circ_0006990 expression was determined using the quantitative real-time PCR in 40 tumor samples and their adjacent non-cancerous tissues. Furthermore, bioinformatics approaches were applied to confirm the roles of this circRNA in RCC.

Results: The expression level of hsa_circ_0006990 decreased in the tumor tissues compared to their adjacent normal tissues. Also, the expression of this circRNA was lower in RCC patients with the tumor size of ≥ 4cm and advanced Fuhrman nuclear grade, that emphasized its tumor suppressive role. Bioinformatics analysis show that hsa_circ_0006990 is a microRNA (miRNA) sponge which could target cell proliferation.

Conclusion: The present study revealed that hsa_circ_0006990 expression is significantly downregulated in RCC tumors, and its lower expression is

associated with larger tumor size and higher Fuhrman nuclear grade. Also, hsa_circ_0006990 could play key roles in the pathology of this cancer through potential key regulatory competing endogenous RNA (ceRNA) functions. However, more studies are needed to determine the exact mechanism of this ncRNA in RCC pathogenesis.

Keywords: hsa_circ_0006990, Renal cell carcinoma, ceRNA, circRNA

Evaluation of the relationship between PH of the umbilical cord artery and short term outcomes in neonates born via normal vaginal delivery in Yas Hospital in 2017 (Research Paper)

Mehrnaz Valadan,[1] Maryam Shamshirgaran,[2] Amir Mirzapour Estabragh,[3,*]

1. Department of Obstetrics and Gynecology, School of Medicine Yas Hospital Tehran University of Medical Sciences
2.
3. Department of Pharmaceutical Biotechnology, Isfahan University of Medical sciences

Introduction: there are so many available methods for evaluating a neonate immediately after birth but most of them are subjective and operator dependent. This study aims to determine the short term outcome of the neonates born with an abnormal ABG after normal vaginal delivery (NVD). Umbilical arterial blood gas (UABG) analysis is more objective than other methods.

Methods: 116 healthy mother with term neonates born via natural vaginal delivery were enrolled and UABG was taken immediately after birth. Outcomes were compared between neonates with an umbilical cord pH less than 7.2 and more than 7.2. P value less than 0.05 was considered as significant.

Results: Results were as fallowing: need for resuscitation (P = 0.162), NICU admission (P = 0.001), convulsion (P = 0.001), start oral feeding less than one hour after birth (chi square=0.001), hospital stay (P = 0.001), Apgar score (P<0.05). None of the neonates died in study groups. So, neonates with PH of the umbilical cord less than 7.2 stay in hospital longer than others, start oral feeding later, have lower APGAR scores, may experience seizure during the first 3 days of their lives, and may admit to NICU. Need for resuscitation is not relevant to PH of the umbilical cord.

Conclusion: An umbilical cord PH can be used as an objective method for evaluating neonates.

Keywords: umbilical, arterial blood gas, neonate, complication.

Evaluation of the therapeutic effects of siRNAs on glioblastoma and siRNA delivery using nanoparticles (Review)

Ava Resae,[1,*]

1. Researcher

Introduction: Glioblastoma multiforme (GBM) is the most aggressive form of brain cancer. Treatment effectiveness and drug delivery for GBM is limited due to the existence of the blood-brain barrier (BBB). SiRNA is a novel treatment modality with potential clinical success. SiRNA can be exploited to inhibit the expression of genes involved in cancer cell survival, migration and multiplication. However, siRNAs are negatively charged and hydrophilic which prohibits them from crossing the BBB. Therefore, they have to be conjugated to other molecules or delivered with nanoparticles, or they will be excreted by kidneys without reaching the brain. As a result, more effective strategies are needed to develop functional siRNAs and deliver them across the BBB to the tumor site.

Methods: In this review article, various nanoparticle-based siRNAs designed for GBM treatment (from 2018-2021) were studied. The keywords “glioblastoma”, “nanoparticles” “siRNA” and “GBM” were searched in PubMed, google scholar and Elsevier, while review articles were excluded. Ninety-five articles were found. Fifteen of them were relevant to our study topic.

Results: Several anti-GBM siRNAs were designed and successfully delivered to the brain through nanoparticles. In one study, a combination of several siRNAs targeting GBM genes (Robo1, EGFR, YAP1, survivin, NKCC1; responsible for GBM cell growth, proliferation, mutation and migration) were loaded into bioreducible poly beta-amino-ester (PBAE) nanoparticles and delivered to the tumor area. This method targeted and silenced multiple genes at once and decreased tumor cell proliferation and migration. Another study administered Aurora kinase B (AKB)-siRNA loaded into lactoferrin nanoparticles to mice, which showed a significant reduction of the tumor mass and invasiveness. Inhibiting DNA damage repair proteins (ATM and DNApk) in radiosensitized GBM cells with siRNA-loaded ECO nanoparticles has also shown to be an effective method in vitro and in vivo. Cationic liposomes are widely used nanocarriers because of their stability and high encapsulation capacity. Their surfaces can easily be modified and various agents such as aptamers or aptamers-like peptides (aptides) can be added in order to enhance siRNA delivery. In addition, due to siRNA being anionic, cationic nanocarriers are better at retaining the siRNA inside. In one study, cationic liposomes loaded with yes-associated protein (YAP)-siRNA demonstrated significant therapeutic effects when combined with gold nanorods. Gold nanorods are effective photothermic agents, which means they can adsorb

light in near infrared (NIR) regions and convert it to heat in the tumor cells and kill them without damaging normal cells. Transferrin magnetic nanoparticles are also potential drug delivery candidates for GBM. They have to be administered along with the application of external magnetic fields around the tumor area in order to enhance the penetration of the siRNA across the BBB. Moreover, transferrin receptors are highly expressed on brain capillary endothelial cells, and using its ligand, transferrin in siRNA delivery can be an effective strategy to penetrate across the BBB. One study showed that multidrug resistance protein-1 (MRP1)-siRNA delivered with polyethyleneimine (PEI)-capped porous silicon nanoparticles, not only inhibited the growth of GBM, but also sensitized the tumor cells further to the effects of chemotherapy. Another study showed that the co-delivery of cisplatin and glutathione peroxidase-4 (GPX4)-siRNA with iron-oxide nanoparticles was highly effective since it led to both apoptosis caused by cisplatin, and ferroptosis caused by iron-oxide in tumor site. Recently, a study developed manganese-containing chitosan-matrix (mNP) nanoparticle that has been able to transfer siRNAs into brain intranasally in mice. The greatest advantages of this method are administration simplicity and non-invasiveness. Finally, PLGA nanoparticles were also used to encapsulate Golgi phosphoprotein 3 (GOLPH3)-siRNAs and deliver them to tumor area which resulted in inhibition of GBM cell growth. In this study GOLPH3 downregulation led to EGFR degradation, which significantly inhibited GBM cell growth.

Conclusion: Taken together, these results suggest that gene silencing by utilizing anti-GBM siRNAs and delivering them to the tumor site by nanoparticles appears to be an effective strategy for treating glioblastoma or inhibiting its progression.

Keywords: glioblastoma, gene therapy, siRNA, brain tumor, nanoparticles

Evaluation of viral concentration methods for enveloped viruses' recovery from wastewaters (Research Paper)

Mohammad tanhaei,[1] Seyed Reza Mohebbi,[2,*] Seyed Masoud Hosseini,[3] Maedeh Rafieepoor,[4] Shabnam Kazemian,[5] Mahsa Saeedi Niasar,[6]

1. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
2. Gastroenterology and Liver Diseases Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences
3. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
4. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
5. Gastroenterology and Liver Diseases Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences
6. Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Introduction: Following the official announcement of the new virus, SARS-CoV-2, and the resulting pandemic, concerns about the shedding of the virus by municipal and hospital wastewater had increased. Usually, methods of concentration viruses from water and sewage samples have usually been able to concentrate unenveloped viruses that are more stable in the environment, such as noroviruses and adenoviruses. Our aim in this study is to investigate different techniques for concentration of enveloped viruses and selecting an optimal one with the highest rate of virus recovery.

Methods: Six different methods were selected based on different principles. Three methods based on the protocol of adsorption-elution with electronegative membranes followed by a re-concentration phase. The fourth method is based on PEG precipitation, the fifth method is flocculation by TGBE, and the last method is direct extraction of samples. To evaluate these techniques, the avian infectious bronchitis (IBV) vaccine isolate was considered as the SARS-CoV-2 model virus for the control process. For this virus, a primer sets based on RT-qPCR SYBR GREEN method were designed to evaluate and quantify the recovery rate of each method. Primers designed with high specificity and sensitivity are able to identify the IBV vaccine strain. To evaluate the methods, we inoculated a certain amount of IBV for each method, along with a non- inoculated sample (negative control sample) and a direct sample of vaccine (positive control sample) were tested.

Results: Of the compared methods, two methods, PEG precipitation and one method based on adsorptionelution, which was a combined method with some modifications, showed higher efficiency in IBV recovery than the other methods. The PEG precipitation method is mostly used for very opaque, low-volume influent wastewater samples.

Conclusion: In this study, some existing methods for concentrating viruses from wastewater to identify and select the optimal method for concentrating enveloped viruses were shown that all methods have the ability to concentrating this type of virus. However, among these methods, PEG precipitation method and the new method, which is a combination of two adsorption-elution methods, showed better results, but due to the larger sample size that can be used for the new method, PEG precipitation can be a better choice. In subsequent analyzes, they also succeeded in concentrating SARS-CoV-2.

Keywords: SARS-CoV-2 . Wastewater . Method . Concentration . Virus

Evaluation the Effect of chronic and acute administration of pregabalin on morphine withdrawal syndrome in rats (Research Paper)

Lida Khodavirdilou,[1,*] Zahra Mehdilou,[2]

1. Tabriz University of Medical Science
2. Tabriz University of Medical Science

Introduction: Effect on excitatory neurotransmitters such as glutamate, P substance is one of the important analgesia mechanisms of morphine. After abrupt discontinuation of morphine consumption, the number of neurotransmitters increases after a while. Pregabalin is evaluated in this study with the hypothesis of reduction of excitatory neurotransmitters.

Methods: Experiments were implemented on rats weighing between 225 and 275 g. in order to create a dependency, morphine injection was performed nine days at doses of 5 mg (Day 1), 10 mg (Day 2 and 3), 15 mg (Day 4 and 5), 20 mg (Day 6 to 7) and 25 mg (Day 8 and 9) per kg subcutaneously twice a day. On the morning of the ninth day, two hours after morphine injection, naloxone was injected at a dose of 4 mg per kg per body weight and was also administrated intraperitoneally, and then signs of withdrawal syndrome such as jumping, movements like a wet dog were recorded for 45 minutes. In the groups treated with pregabalin(acute) medicine after injection of morphine, the medicine was injected in three doses of 10, 5, and 2.5 mg per kg of body weight through the intraperitoneal method ninth day and an hour after injecting the last dose of morphine. In chronic use, after daily morphine injection, the drug was dissolved in the carrier at doses (10,20,40 mg/kg) and administered half an hour after morphine injection.

Results: According to the recorded results, In case of acute use in doses of 10 and 5 mg/kg ($p < 0.001$) and in case of chronic use in two doses 40.20 mg/kg ($p < 0.001$) compared to the control group (morphine) most of the symptoms such as jumping, gestures like wet dog, teeth chattering were less severe.

Conclusion: The results show that pregabalin in both acute and chronic methods, in these two doses, significantly reduced the symptoms of morphine withdrawal syndrome.

Keywords: pregabalin, withdrawal syndrome, morphine.

Evaluation the Effect of Thiosemicarbazones complexes (Ni) on Expression Changes of LncRNA CASC15 in Acute lymphoblastic leukemia (Jurkat E.6.1) (Research Paper)

Arezoo Hassani,[1,*] Golnaz Asaadi Tehrani,[2] Sina Mirza Ahmadi,[3]

1. Islamic Azad University, Zanjan, Iran.
2. Islamic Azad University, Zanjan, Iran.
3. Islamic Azad University, Zanjan, Iran.

Introduction: Acute lymphoblastic leukemia is a type of leukemia, which is most current in children. ALL involves lymphocyte cells and contains about 30% of childhood cancers. thiosemicarbazones complexes are range of chemical compounds that have antitumor activity. Their antitumor activity is related to inhibition of ribonucleotide reductase (RNR), reactive oxygen production, inhibition of topoisomerase II, mitochondrial dysfunction and inhibition of multiple drug resistance protein (MDR1). The purpose of this study was to evaluate the effect of thiosemicarbazones complexes with Ni metal ions on expression changes of LncRNA CASC15 in the acute lymphoblastic leukemia Jurkat E6.1 cell line.

Methods: In this study, different concentrations of thiosemicarbazones complexes (Ni) were examined with the MTT test. Then thiosemicarbazones complexes (Ni) were prepared at 51 and 61µM concentrations. The Jurkat E6.1 cell line (Acute lymphoblastic leukemia) was treated by Ni at 48 hours after cell passage. Then RNA extraction and cDNA synthesis were performed and the expression changes of LncRNA CASC15 and GAPDH as the Housekeeping gene were evaluated by Real Time PCR. Finally, the results of Real Time PCR were analyzed by Rest 2002 Software.

Results: The Results of the research showed that the expression of LncRNA CASC15 significantly decreased after treatment with thiosemicarbazones complexes (Ni) at 51 and 61µM concentrations in 48 hours compared with non-thiosemicarbazones complexes (Ni) samples (as a control groups, p-value < 0.001). Conforming to the results, it has been found that concentrations of 51 and 61µM Ni in 48 hours are the optimal concentrations and time of the effect of this drug. The expression of LncRNA CASC15 at the indicated concentrations and time were 0.714 and 0.992.

Conclusion: According to the results of the study of expression changes in LncRNA CASC15 under thiosemicarbazones complexes (Ni) treatment, it can be concluded that both concentrations of the drug were effective in reducing the expression of LncRNA CASC15. The results showed at the concentration of 51µM of Ni drug, a further decrease in expression of LncRNA CASC15 was

observed, which is the most effective concentration of the drug. Overall, thiosemicarbazones complexes (Ni) had a positive effect on the LncRNA CASC15 oncogene reduction process over a period of 48 hours and at the studied concentrations, this decrease in expressions was statistically significant (p-value < 0.001). Evidence suggests that the thiosemicarbazones complexes (Ni) has high potential for cancer control and treatment.

Keywords: LncRNA CASC15, GAPDH, Housekeeping, cDNA, thiosemicarbazones complexes

Evaluation the effect of ZnO nanoparticle derived Bacillus subtilis on the expression of efflux pump genes (AdeB AdeRS) in Acinetobacter baumannii (Research Paper)

Fatemeh Saleh,[1,*] Farnaz Kheirandish,[2] Farzaneh Hosseini,[3] Fatemeh Yazdian,[4] Atefeh Mirderikvand,[5]

1. Razi Herbal Medicine Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran
2. Department of Medical Parasitology and Mycology, School of Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran, Department of Medical Biotechnology, School of Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran
3. Department of Microbiology, Islamic Azad University, Tehran North Branch, Tehran, Iran
4. Faculty of New sciences and Technologies, University of Tehran, Tehran, Iran
5. Razi Herbal Medicine Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran

Introduction: Green approach to the nanoparticles, including metal oxides due to inevitable disadvantages of physical or chemical synthesis routes is attractive nowadays. Zink oxide (ZnO) nanoparticles play a key role in the medical and pharmaceutical fields. This research aimed to study the biologically synthesized ZnO nanoparticle using Bacillus subtilis, and evaluated its antibacterial properties.

Methods: Bacillus subtilis culture in a broth nutrient environment was used, followed by adding the Zinc acetate dehydrate. Biosynthesis of the nanoparticles was confirmed by the XRD, FTIR, and SEM imaging. The antibacterial effects of NPs on the expression of AdeB efflux pump genes and the AdeRS regulator were studied; clinical species of the Acinetobacter baumannii were collected from clinical samples of Khorramabad, using the phenotypic (MIC) and the genotypic methods through real-time PCR.

Results: X-ray diffraction pattern (XRD) result showed, that all of the peaks were related to the ZnO, and no other peaks were detected; it also demonstrated nanostructure nature with crystallite size of 25–50 nm. The results indicated, that the antibacterial properties of the nanoparticle increased the AdeRS expression and decreased the AdeB expression in 40% of the A. Baumannii. In addition, there was an increase in the AdeB expression in 60% of the species, indicating an increased probability for mutation.

Conclusion: Given the desirable inhibitory effects of biosynthesized ZnO NPs on the expression of AdeB and AdeRS, which play an important role in the pharmaceutical resistance of Acinetobacter species, it seems that ZnO NPs can be used as a medication candidate in pharmaceutical industry in the future.

Keywords: Znic oxide nanoparticle . Biological synthesis . Gene regulation . Multiple drug resistance . Real-t

Evaluation the immunity of Neospora caninum attenuated strain in preventing oocyst shedding in dogs (Research Paper)

Elham Ghazanfari,[1] Ahad Olyaei,[2] Mohammad mehdi Namavari,[3,*] zahra khabazan,[4]

1. Department of Veterinary Medicine, Kazerun Branch, Azad University, Iran
2. Department of Veterinary Medicine, Kazerun Branch, Azad University, Iran
3. Shiraz Branch, Razi Vaccine and Serum Research Institute, Agricultural Research, Education and Extension Organization (AREEO), Shiraz, Iran
4. Shiraz Branch, Razi Vaccine and Serum Research Institute, Agricultural Research, Education and Extension Organization (AREEO), Shiraz, Iran

Introduction: The protozoan Neospora caninum is known around the world as one of the most important causes of disaster abortion in cattles, especially when the dogs live as the main host in their surroundings. Currently, the focus is on live vaccines or attenuated vaccines. In this research; Neuspora caninum has been evaluated as an effective vaccine to prevent oocyst shedding in dogs.

Methods: Sixteen dogs were randomly divided into four equal groups, including the live-attenuated strain without adjuvant, acute strain, live-attenuated strain with oily adjuvant, and the control group. All the groups were immunized in two phases, four weeks apart. One month after the second injection, all dogs were challenged by acute NC-1 strain. Agglutination test was used to assess the immune response and molecular test was used to assess oocyte shedding.

Results: The results showed that the immunized group with live-attenuated strain with adjuvant produces the highest immune response. PCR test also showed that dogs immunized with live-attenuated strain with adjuvant did not shed oocyst after challenge. Overall, the results of this study showed that Neuspora caninum live-attenuated vaccine with oily adjuvant in dogs is effective in creating an immune response and controlling oocyst shedding, and immunizing with this method is safe and completely effective.

Conclusion: Therefore, it is suggested that this experimental vaccine will be used in supplementary research in order to obtain a functional vaccine to control the infection caused by Neospora caninum in dogs.

Keywords: Neospora caninum, dog, oocyst shedding, immunization

Evaluations of the challenges and benefits of using Pegylated doxorubicin liposomal form to reduce cardiac toxicity in patients with metastatic breast cancer (Review)

Zahra Farhoud Khomeirani,[1,*] Sepehr Bozorgchenani,[2]

1. Department of veterinary, Rasht Branch, Islamic Azad university
2. Department of Bioinformatics, Tehran branch, Science and Culture University

Introduction: Breast cancer is metastatic cancer and can usually spread to distant organs such as bones, liver, lungs, and brain, mainly due to incurable causes. Early detection of the disease can lead to a good prognosis and a high survival rate. In the early stages of breast cancer, surgery alone can cure the patient, later adjuvant chemotherapy agents are planned to treat the micrometastatic stages. Despite demonstrating the benefits of chemotherapy agents in reducing the incidence of recurrence in breast cancer patients, a significant number of early-stage breast cancer patients develop an incurable metastatic disease. In this study, we investigate the proposed mechanisms of anti-cancer effects of doxorubicin, especially the liposomal form of pegylation to reduce cardiac toxicity in patients with metastatic breast cancer.

Methods: In this study, we searched for the effects of the (PLD) on breast cancer in Pubmed, Google Scholar, Online Wiley, and Springer databases.

Results: The reduction of cardiac toxicity in the liposomal form of PEGylated doxorubicin PLD has led to new side effects. Studies have shown that mucositis and PPE are the two most common complications of PLD. Given the current findings, future studies must increase the number of patients to increase conclusive results and stronger evidence of adverse events and the relationship between treatment plan, patient age, pretreatment, and adverse events.

Conclusion: Doxorubicin (DOX) is one of the leading treatments for early and advanced breast cancer. The resulting cardiac toxicity necessitates new forms to reduce the risk of disease associated with the drug. One of the most promising strategies designed to reduce these effects is to use nanoparticles as potential drug nanocarriers to facilitate a particular drug, to increase efficacy while minimizing the adverse effects of chemotherapy. Cardiotoxicity in the use of doxorubicin, the liposomal form of doxorubicin pegylated, by reducing the pharmacokinetics of the drug, reduces side effects compared to conventional drug treatment.

Keywords: Metastatic breast cancer, Doxorubicin, PEGylated liposomal doxorubicin, anti-cancer

Examining the knowledge and attitudes about masturbation and the risks in medical sciences students (Kermanshah-Iran, 2020) (Research Paper)

Mohammad Amin Rezaei,[1,*] Mohammad Rasool Khazaei,[2]

1. Student Research Committee, Kermanshah University of Medical Sciences, Kermanshah, Iran
2. Fertility and Infertility Research Center, Health Technology Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran

Introduction: Masturbation is to mechanically stimulate the sexual organs, which is a physiological phenomenon according to some researchers. Being a taboo and due to the lack of knowledge about this issue, the youth have to deal with several problems about masturbation. Having indigenous, accurate, and specially designed tools to measure the knowledge about the risks and attitudes to masturbation is highly important.

Methods: This descriptive study was carried out on male medical sciences students at Kermanshah University of Medical Sciences (basic sciences program) in 2019-2020. Through convenient sampling, 87 participants entered the study. Data gathering tool was a researcher designed tool with 35 items about knowledge of the risks and outcomes and attitudes about masturbation. The items were designed based on Likert's four-point scale. Face validity of the tool was supported by 10 experts and the tool was provided to 15 students as pilot group to find and remove the weaknesses in the tool. After data gathering, four questionnaires were excluded for being incomplete. Data analyses were done in SPSS (v.22) using descriptive statistics (frequency, mean).

Results: The answers "completely agree" and "agree" were assumed as agreement of the participants about the risks of masturbation. The specifications with which more than 75% of the students were agree were detectability of masturbation habitsthroughout recruitment examinations, sterilization, changes in testicle size, muscular degradation, premature ejaculation, decrease in the quality and quantity of sperms, detectability of masturbation behaviors through sonography, risk of prostates cancer, losing hair, eyesight impairment, dark circles under the eyes, severe protein loss, decrease in learning performance, depression, anxiety, physical weakness, backpain, guilt, lordosis, and losing facial beauty.

Conclusion: There is an urgent need to inform students about the risks of masturbation.

Keywords: Masturbation, medical, Kermanshah

Exo-circRNAs: a novel potential target for cancer diagnosis and treatment (Review)

Roqaye Karimi,[1,*] Amir Atashi,[2] zahra sadat mousavi,[3] Monireh Ajami,[4] Mansoureh Ajami,[5]

1. Department of Hematology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran
2. Stem cell and Tissue Engineering Research Center, Shahroud University of Medical Sciences, Shahroud, Iran
3. Student Research Committee, Shahroud University of Medical Sciences, Shahroud, Iran
4. Department of Medical Laboratory Sciences, School of Paramedical Sciences, Islamic Azad University Tehran Medical Sciences, Tehran, Iran
5. Department of hematology, School of Allied Medical Sciences, Shahroud University of Medical Sciences, Shahroud, Iran

Introduction: Exosomes are extracellular vesicles secreted by most cells in interstitial spaces and biological fluids and usually have a diameter of 30-100 nanometers. They are important mediators of interactions between various cells and can change the behavior of the target cells. Exosomes contain a variety of molecules, including proteins, lipids, DNA fragments, miRNAs, LncRNAs, and circRNAs. It's interesting that tumor cells secrete exosomes about 10-fold higher than other cells, and exosomal circRNAs (exo-circRNAs) are reported to have a significant role in the formation and progression of cancer through cell division, metastasis, and drug resistance.

Methods: The present study aimed at reviewing related scientific articles to examine and analyze the mechanism of drug resistance and chemoresistance in malignant tumors such as colorectal cancer (CRC) and the role of exo-circRNA in the development of chemoresistance in cancer cells. in this study, numbers and sizes of exosomes were examined by Nanoparticle tracking analysis (NTA) and exosomal RNA was detected by RT-qPCR. Using tumor-implanted mice, the impacts of exo-circRNA derived from chemoresistant tumors on nonchemoresistant tumors in vivo were investigated. TargetScan, starbase and RNAhybrid were used for bioinformatics analyses. In the oxaliplatin-resistant cell line, siRNA of PKM2 or ciRS-122 was transfected to downregulate the expression level of PKM2 or ciRS-122 in vitro, and mouse xenograft models were used to show that exosome-delivered si-ciRS-122 could increase the susceptibility of tumors to oxaliplatin in vivo.

Results: The exosomes of chemoresistant CRC cells contained ciRS-122 circRNA which was found to be a sponge for miR-122. On the other hand, PKM2 led to increased glycolysis and energy production in these cells.

Furthermore, upregulation of PKM2 gave transporters more energy to expel drugs from CRC cells. The researchers also showed that the exosomes of chemoresistant cells delivered ciRS-122 to chemosensitive cells, eventually increasing glycolysis and drug resistance in these cells. The important point is that the researchers succeeded to remove ciRS-122 using exosome-delivered si-ciRS-122, eventually lowering PKM2 levels and increasing miR-122 levels, and also increasing the sensitivity of CRC cells to oxaliplatin in mice. This represents a potential new approach to reversing oxaliplatin resistance in CRC.

Conclusion: According to the results of the present study, exosomes played an important role in the development of chemoresistance in drug-sensitive cells by transferring circRNA. This intercellular signal transduction introduces a new therapeutic target for overcoming chemoresistance in tumors and may provide a basis for future clinical therapies for drug-resistant cancer cells. On the other hand, delivery of tumor suppressor circRNAs or the circRNAs encoding therapeutic proteins to exosomes could be a new cancer treatment method interested by many researchers today. Furthermore, early detection of a number of cancers is difficult due to the lack of accurate and appropriate biomarkers. Thus, identifying accurate and sensitive biomarkers to diagnose cancer seems necessary. Considering that exo-circRNAs are more stable and protected than miRNAs and other ncRNAs and have long half-lives as well as tissue-/cell-specific patterns, they can be used as potential biomarkers for early detection of cancer and response to treatment.

Keywords: circRNA, exosome, chemoresistance, drug resistance, cancer

Exosome therapy for COVID-19 infection (Review)

Mahsa Rahgoshay,[1,*] Amir Atashi,[2] Mansoureh Ajami,[3] Fatemeh Jamshidi,[4]

1. Department of Hematology and Medical Laboratory Sciences, Faculty of Allied Medicine, Kerman University of Medical Sciences, Kerman, Iran
2. Department of Medical Laboratory Sciences, School of Allied Medical Sciences, Shahroud University of Medical Sciences, Shahroud, Iran
3.
4.

Introduction: first detected in Wuhan, China. Since December 2019, the outbreak of disease has become a serious global health threat. The number of confirmed Covid-19 patients stands at more than 220 million people globally, with over 4 million deaths and more than 200 million cases have recovered. COVID-19 primarily affects the lungs and the infection may progress and cause life-threatening complications induced by a cytokines storm including pneumonia, acute respiratory distress syndrome (ARDS), septic shock, multi-organ dysfunction, and even death. There are no specific antiviral medications for COVID-19 virus-infected patients to date. Finally, an effective vaccine will be required to offer protection against SARS-CoV-2 infection. However, with unprecedented efforts being made by scientists, few vaccines have been approved by the FDA. Although the vaccination protects the receiver from suffering a serious disease, there is no evidence so far that the vaccine prevents the virus from spreading indefinitely. In this regard, there is a rapid pace of clinical examinations to find promising therapeutic strategies for the disease. Some approaches using human mesenchymal stem cells (MSCs) and/or MSC-derived Extracellular Vehicles (EVs) as a therapeutic solution for the treatment of severe COVID-19 patients. Although promising results of MSCs transplantation have been demonstrated extensively, this technique is restricted owning to cell viability, safety, scalability, and some regulatory problems, making it an impractical choice for millions of infected cases around the world. However, EVs secreted from MSC, a crucial set of signaling encapsulated vesicles, are novel, next-generation agents that have similar functions as their parent cells.

Methods: EVs may have a role in preventing the cytokine storm and also avoiding the suppression of antiviral defenses that were responsible for COVID-19 pathogenesis. Among EVs, the prominent roles of exosomes in different pathological conditions have been widely reported. Exosomes are membrane-bound EVs 30–120 nm in size and may be involved in both pathological and physiological conditions. In the last year, several pre-clinical studies have confirmed that EVs-based therapies, particularly MSC-derived exosomes (MSC-Exo), considerably attenuated pulmonary inflammation and improved the clinical function of damaged lungs in a rapid, and safer way.

Moreover, MSC-Exo might play a crucial role in the control of acute respiratory impairment induced by coronaviruses. Multiorgan dysfunction has been seen in many infected patients with COVID-19. According to the clinical reports, MSC-Exo contains a variety of growth factors, cytokines, mRNA, and miRNA with regenerative potential and anti-inflammatory and immunomodulatory effects which can repair diverse experimental injury models like liver injury, CNS stroke, renal injury, cardiovascular, and various types of lung disease. Therefore, they could be a good tool to treat multiple organ dysfunction. Furthermore, sepsis is a key lethal disease in COVID-19 patients, and MSC-Exos has the potential to reduce the rate of death in animals with sepsis. Several studies have shown that miRNAs secreted by MSC-Exo like miR-145, miR-21, and let-7 accelerate lung recovery. Moreover, miRNA could change the expression of cell receptors and thus blocking RNA viruses like Coronavirus to enter the cells. A recent study by Sengupta et al. concluded that exosomes derived from bone marrow mesenchymal stem cells (ExoFlo™) could potentially treat severe COVID-19.

Results: The data revealed a survival rate of about 83%. 71 % of the cases recovered, 13 % remained critically ill, and 16 % expired for causes unrelated to therapy. Moreover, laboratory values have shown a reduction in C-reactive protein (CRP) and D-dimer concentration, with a remarkable improvement in neutrophil and lymphocyte count. Generally, exosomes may be considered as an alternative to MSCs, because they can readily cross the blood-brain barrier, are economical, and don't undergo independent self-renewal, so avoiding adverse effects, such as tumor development.

Conclusion: Finally, although MSC-Exosomes appears to be an intriguing COVID-19 therapeutic agent, additional investigation is needed for their clinical application. Moreover, it is imperative to optimize exosome isolation, storage, optimum dosage, and route of administration for the treatment of COVID-19 patients. As a result, since MSCs have been researched more extensively in these fields than MSC-Exos, they are predominantly examined in COVID-19 clinical trials.

Keywords: COVID-19; Mesenchymal stem cells; Extracellular vesicles; Exosomes; Cytokine storm

Exosomes : a novel method for cancer therapy (Review)

Nazanin Rahmani ,[1] ,*

1. Shandiz institute of higher education

Introduction: Extracellular vesicles (EVs) are lipid bound vesicles secreted by cells into the extracellular space. EVs contain of lipids, nucleic acids, microRNAs (miRs), and proteins—specifically proteins associated with the plasma membrane, cytosol, and those involved in lipid metabolism. For therapeutic purposes of EVs, we must define intrinsic characteristics such as circulation kinetics, targeting, internalization and intercellular trafficking routs, is needed to fully exploit these features of EVs for therapeutic purposes.

Methods: Although EVs play an important role in intracellular communication, we still do not have much information about the regulation of cardiomyocyte's EVs. According to previous research a large number of deaths are due to cardiovascular disease and cancer. Also recent studies indicated EVs are involved in many physiological and pathological cardiovascular processes including: the regulation of angiogenesis, blood pressure and cardiac fibrosis. Furthermore, EVs possess numerous advantageous features as drug delivery vehicles that may help them to perform better than synthetic drug carriers. Notably, EVs have an intrinsic ability to cross tissue and cellular barriers. EVs have been successfully utilized as a drug delivery system in preclinical settings.

Results: The advantage of using EV over cell therapy is that depending on their source may be less immunogenic than their parental cells likely due to lower abundance of transmembrane protein such as MHC complexes on their surface. Unlike living cells, they have a long term of life and can carry and store cargo for a long time. Compared with free formulation of drugs, EV-mediated delivery indicates enhanced capacity to penetrate through tumor blood vessels and across biological barriers to accumulate at tumor sites, which greatly improve their therapeutic efficacy. This review provides an overview of Extracellular vesicles (EVs) with a focus on the potential of EVs to enhance their therapeutic application.

Conclusion: Finally EVs do not proliferate after injection, so EVs have a lower risk of developing tumors and transmitting latent viral pathogens.

Keywords: exosome , cancer , diagnostic test, cardiovascular disease , microRNA

Expression analysis of StAR gene in rats with polycystic ovarian syndrome and hypothyroidism induced by PTU (Research Paper)

Sara Khodabandeh,[1,*] Homayoun Khazali,[2] Vahid Azizi,[3] abdolkarim hosseini,[4]

1. Faculty of Life Sciences and Biotechnology, Shahid Beheshti University
2. Faculty of Life Sciences and Biotechnology, Shahid Beheshti University
3. Faculty of Life Sciences and Biotechnology, Shahid Beheshti University
4. Faculty of Life Sciences and Biotechnology, Shahid Beheshti University

Introduction: Thyroid disorders and polycystic ovarian syndrome(PCOS) are two of the most common endocrine disorders. Although their pathophysiology are different, but they have similar features; for instance, they both show increase size of ovary and cystic appearance of ovary. PCOS is the most common cause of infertility in reproductive age women. Early diagnosis can help avoid the aggravation of PCOS. Gynecologist can tell PCOS from the symptom description by the patients (such as the history of oligomenorrhea), and morphological features (hirsutism). However, PCOS diagnosis is based on some pre-defined criteria. In 1990, a conference convened by National Institutes of Health (NIH) defined the signs and symptoms of PCOS, which served as the original diagnostic criteria. Rotterdam consensus workshop held in 2003 characterized hyperandrogenism, menstrual irregularities and insulin resistance as the key features of PCOS. Blood pressure, cycle duration, follicle count, mean ovarian volume, SHBG, testosterone, FSH and prolactin can indicate PCOS. Thyroid disorders are the most common endocrine problems in women. Among various thyroid disorders, the prevalence of hypothyroidism is more with about 4%–5% worldwide. Females are at more risk of developing hypothyroidism than males. Undiagnosed and untreated thyroid disease can be a cause for infertility as well as sub-fertility. Thyroid dysfunction can affect fertility in various ways resulting in anovulatory cycles, luteal phase defect, high prolactin (PRL) levels, and sex hormone imbalances. There are researches that indicate how PCOS women can get hypothyroidism and also some researches show how hypothyroidism can cause PCOS. Nevertheless it is not clear how these two diseases can affect each other which is the aim of this study.

Methods: 25 female wistar rats were divided into 5 groups (n=5): 1)control, 2)PCOS group, 3)PCOS + PTU1, 4)PCOS+ PTU2, 5)PCOS+PTU4. PCOS was induced with estradiol valerate (2mg/kg). after 30 days groups 3 , 4 and 5 were feed with 1 , 2 and 4 mg/kg propylthiouracil for 7 days. After that both ovaries were isolated for measurement of StAR gene expression. Data were analyzed by Graph Pad Prism8 software and appropriate tests.

Results: qRT-PCR results showed StAR expression was significantly higher in PCOS group than control Group and also its expression was significantly lower in PTU groups that received 2 and 4 mg/Kg than PCOS group.

Conclusion: Disruption of StAR expression is the causative factor that effect steroidogenesis. Since measurement of steroid hormones is one of the way for diagnosis of PCOS , so occurrence of both hypothyroidism and PCOS make it harder to diagnose PCOS and following that it would be harder to deal with these diseases.

Keywords: StAR gene, Hypothyroidism, PCOS

Expression analysis of MEF2C mRNA levels in breast cancer (Research Paper)

Zeynab Shaghaghi Torkdari,[1] Mohammad Khalaj-Kondori,[2,*] Mohammad Ali Hosseinpour Feizi,[3] Vahid Montazeri,[4]

1. University of Tabriz
2.
3. University of Tabriz
4. Tabriz university of medical sciences

Introduction: This study aimed to evaluate the mRNA levels of MEF2C in tumor and adjacent non tumor tissues of 70 (younger and older than 40 years) women with invasive ductal carcinoma as well as three breast cancer cell lines. The association of MEF2C expression and the clinical characteristics of patients have also been investigated.

Methods: MEF2C mRNA levels were studied by Real time PCR and data were analyzed by T-test and ANOVA.

Results: Low levels of MEF2C mRNA were observed in tumor tissues compared with adjacent non tumor tissues ($P<0.001$). In addition, the results show that patients with large tumors and positive lymph node metastasis have low levels of MEF2C mRNA ($P<0.05$).

Conclusion: The low mRNA levels of MEF2C in breast cancer patients possibly associated with lymph node metastasis and larger tumor size.

Keywords: MEF2C, Downregulation, Breast cancer

Expression of soluble human interleukin 1 receptor antagonist in SHuffle T7 express E. coli" (Review)

Sanaz Sedghi Esfahani,[1,*]

1. Royan Institute

Introduction: Cytokines are a large group of proteins or peptides. There are two groups of cytokines, including pro-inflammatory and anti-inflammatory. Among different cytokine proteins, IL-1 (Interleukin-1) and TNFα (Tumor necrosis factor) have the highest rate of inflammatory activity. IL-1 is a dominant pro-inflammatory cytokine that activates the immune response against infections through stimulation of B and T lymphocytes and reduces the number of white blood cells. This cytokine also causes fever, and lowers the blood pressure. IL-1 is consist of seven ligands including IL-1α (Interleukin-1α) and IL-1β(Interleukin-1β) and IL-1 receptor antagonist (IL-1RA). This antagonist is naturally produced by monocytes, macrophages and neutrophils with essential functions in prevention of inflammation, mainly in artrit rheumatoid. IL-1 receptor consists of two subunits including IL-1RI (Interleukin-1receptor I) and IL-1RAcP (Interleukin 1 receptor accessory protein). However, IL-1RA binds to the IL-1RI subunit with higher binding affinity compared to IL-1α or IL-1β (Interleukin-1 β), it is unable to recruit the IL-1RAcP Subunit, so the signaling pathways are not activated. Hence, the expression of downstream target genes related to the inflammatory signaling including IL-1, IL-6 and TNFα is not induced, the activation of inflammatory responses is prevented. Accordingly, the therapeutic application of recombinant human IL-1RA leads to reduce the inflammatory symptoms of the autoimmune disease such as rheumatoid arthritis, infectious diseases, and some cancers particularly leukemia. Furthermore, recent studies revealed that a number of patients with a confirmed infection caused by novel coronavirus in France and Italy, treated with recombinant human IL1-RA, called Anakinra, had improved clinical symptoms such as lower hypoxia, fewer days depending on the ventilator and also rapid decrease of fever. Considering the therapeutic significances of IL1-RA, in the present study, we aimed to produce the soluble form of human recombinant IL-1RI as a bio-active protein in SHuffle T7 express E. coli. For this purpose, an expression cassette containing the coding sequence of human IL-1RA derived by T7 promoter, was cloned into pET15b that contained the expression cassette of Trxa(Thioredoxin) was previously constructed, as an un-fused solubilizing tag. His tag was also inserted upstream of the IL-1RA coding sequence, facilitating the protein purification with Ni-NTA resin. Moreover, for removal of His tag post purification, we included TEV protease recognition site downstream of the His tag sequence. The co-expression of thioredoxin was successfully resulted in soluble expression of human IL1-RA protein and prevention of inclusion body formation at 4h, 30°C and 0.5 mM IPTG.

Methods: In this study, we isolated RNA from human blood cells and synthetized total cDNA, and then human IL-1RA CDS was amplified using appropriate primers. After that it was cloned into pET15b/TrxA vector to construct recombinant plasmid pET15b/ IL-1RA/Trxa. The plasmid sequenced for the accuracy of the sequence of IL-1RA. After ensuring the correct sequence, then co-expression IL-1RA and TrxA uder control T7 promoter. Finally, vector was transformed into SHuffle T7 express E. coli strain and next transformed bacteria were cultured in LB medium containing ampicillin, supplemented with IPTG for co-expression of IL-1RA and TrxA. The produced human recombinant IL-1RA was purified with Ni-NTA agarose and analyzed with 12% sodium dodecyl sulfate–polyacrylamide gel electrophoresis (SDS-PAGE). Eventually, different induction conditions were also evaluated for obtaining the best condition.

Results: The recombinant vector named pET15b/IL-1RA/TrxA was successfully constructed. After the vector transformation into SHuffle T7 express E. coli the production of recombinant IL-1RA was induced using IPTG. Fortunately, a large amount of the soluble recombinant protein was obtained after 4 hours of induction, which was purified using affinity purification method via Ni-NTA Agarose resin.

Conclusion: We constructed a IL-1RA-expressing plasmid that successfully expressed in soluble form of human IL-1Ra protein. After transformation into SHuffle T7 express E. coli, the results showed that the expressed recombinant IL-1Ra was produced in soluble form with remarkable expression rate in optimized induction condition and was efficiently purified with N-terminal His-tag via Ni-NTA.

Keywords: Human IL-1RA, Recombinant protein, Shuffle T7 express E. coli, Thioredoxin, Ni-NTA.

Expression of the HIV-1 Nef-Vif fusion protein in E. coli strain (Research Paper)

Fateme shahhosaini,[1,*] Azam Bolhassani,[2] Neda Mousavi-Niri,[3]

1. Department of Biotechnology, Faculty of Advanced Science and Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran
2. Department of Hepatitis and AIDS, Pasteur Institute of Iran, Tehran, Iran
3. Department of Biotechnology, Faculty of Advanced Science and Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

Introduction: The development of an effective vaccine against the human immunodeficiency virus (HIV)-1 is a global health priority. Fusion recombinant vaccines have several potential benefits which could be applied in the case of mutable divergent pathogens. HIV-1 is a complex retrovirus containing 15 different proteins which play key roles in the virus's pathogenicity. Since accessory proteins of HIV-1are critical throughout the infection, a fusion recombinant protein containing the full length of HIV-1 Nef and Vif was expressed in E. coli Rosetta strain.

Methods: At first, cloning of the Nef-Vif fusion gene was performed in the pET24a (+) expression vector. Then, the recombinant Nef-Vif protein was expressed in Rosetta E. coli bacteria using IPTG inducer in different conditions. Finally, the protein expression was confirmed by SDS-PAGE and western blotting.

Results: The recombinant pET24a (+)-Nef-Vif vector was confirmed by enzymatic digestion and PCR demonstrating a clear band of ~ 1200bp related to the Nef-Vif fusion gene conducting agarose gel electrophoresis. SDS-PAGE and Western blotting confirmed the expressed protein as a clear band of ~50 kDa at 16 h after induction with 1mM IPTG.

Conclusion: Considering the important roles of Nef and Vif in virus infectivity, the construction of Nef-Vif fusion gene was performed in a prokaryotic expression vector to express the Nef-Vif fusion protein in E.coli strain under certain conditions. This protein will be purified in progress to develop a protein-based HIV-1 vaccine candidate in future.

Keywords: AIDS, HIV, Nef, Vif, Recombinant protein

Expression patterns of CD200 and CD160 in leukemic B-cell chronic lymphoproliferative disorders and their potential value in the differential diagnosis (Research Paper)

ATEFE RAHMATI,[1] MOHAMMADHADI SADEGHIAN,[2,*] HOSSEIN AYATOLLAHI,[3] FIROOZE SOLEIMANI,[4]

1. Department of Hematology and Blood Banking, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
2. Department of Hematology and Blood Banking, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
3. Cancer Molecular Pathology Research Center, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
4. Department of Medical Biotechnology and Nanotechnology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

Introduction: Chronic lymphocytic leukemia (CLL) is usually diagnosed based on morphology and immunophenotype, and usually, it presents no problems from a diagnostic standpoint. However, in some patients, overlapping immunophenotypes or variations in the expression or intensity of expression of scoring markers do exist and raising the diagnostic uncertainty. The present study aimed to investigate the diagnostic benefit of measuring CD200 and CD160 markers in chronic B-cell lymphoproliferative disorders (B-CLPDs).

Methods: Using flow cytometry analysis, the expression of CD200 and CD160 was investigated in 64 consecutive patients with B-cell chronic lymphoproliferative disorders (B-CLPD) (82 CLL, 42 other B-cell neoplasms) in addition to 11 controls. CD200 and CD160 were analyzed as a percentage of positive cells (≥20%) and the ratio between the mean fluorescence intensities (MFIs) of CLL B-cells/ negative lymphocyte populations and were considered positive when the ratios were ≥2 and 20, respectively.

Results: Ninety-five and forty-one percent of CLL patients expressed CD200 and CD160 compared to five and ten percent of other adult B-cell neoplasms ($p<0.001$, $p=0.004$). Concurrent expression of both markers was observed in more than 40% of CLL patients and only in the other five percent of adult B-cell neoplasms. Lack of expression of both markers occurred in 5% of CLL patients but 67% of other adult B-cell neoplasms. The results of this study showed that CD200 and CD160 expression in patients with CLL were upregulated.

Conclusion: Altogether, evaluation of CD200 and CD160 expression pattern can be valuable, albeit not specific, in the differential diagnosis of atypical CLL from other B-CLPD in the absence of further explorations.

Keywords: Chronic lymphocytic leukemia, Immunophenotyping, CD200, CD160

Fabrication and Characterization of anti-coagulant loaded nanofibrous PLLA and PET scaffolds for Vascular Tissue Engineering Applications (Research Paper)

Mahboubeh Kabiri,[1,*] Saba Aslani,[2] Romina Sepehri,[3] Chakavak Nojavan,[4] Payam Zahedi,[5]

1. Department of Biotechnology (straight Ph.D), College of Science, University of Tehran
2. Department of Biotechnology (straight Ph.D), College of Science, University of Tehran; Department of Neurology and Neurosurgery, McGill University, Quebec, Canada
3. University of Tehran
4. University of Tehran
5. University of Tehran

Introduction: The number of patients in need for vascular bypass grafting surgery is dramatically increasing, highlighting the development of functional small-diameter vascular grafts. Nevertheless, the high incidence of occlusion of tissue-engineered vascular grafts has remained a main challenge, leading to broad research in this specific field with a focus on construction of higher biocompatible grafts to inhibit or diminish blood clot formation. Local application of anti-coagulant agents can provide local anti-thrombotic effects.

Methods: Herein, in a series of studies we fabricated electrospun nanofibers from poly-L-lactic acid (PLLA) and poly-ether-sulfone. The PLLA scaffolds (Aligned or Random) were surface coated with Amniotic Membrane (AM) lysate for enhanced biocompatibility; and PET scaffolds were integrated with either carbon-nanotubes (CNT) or graphene oxide (GO) to make conductive substrates for endothelial cells attachment. Composition and ratios of the scaffolds were first optimized and the fabrication process was optimally developed. Also, we incorporated two main anti-coagulant agent (Aspirin and Heparin) in the fibers and assessed drug loading and release pattern into and out of the nanofibers, aiming to provide a local anti-coagulant releasing vehicle, directly inside the vascular grafts, where platelets would come across to and get activated. All three nanofibrous scaffolds were structurally and mechanically characterized and assessed for cyto- and hemo-compatibility.

Results: All different vascular constructs showed to have uniform, bead-less morphology with the fibers being in the range of nanometer. Plasma treatment made the scaffolds acceptingly hydrophilic and suitable for cell attachment. Anti-coagulant release profile showed a burst release followed by a constant release pattern over a 24-hour time window. The number and morphology of the platelets, assessed by SEM confirmed anti-activating and anti-platelet adhesion effects of drug loaded scaffolds compared to bare controls

Conclusion: Overall, our results together indicated that aspirin/heparin releasing PLLA and PET/GO PET/CNT scaffolds have appropriate physical and biochemical characteristics needed for a vascular graft with promising potential for further research towards development of the desirable small diameter vascular graft.

Keywords: Vascular Tissue Engineering, Anti-coagulant, Thromboses, Scaffold, Aspirin, Heparin

Factors associated with domestic violence during pregnancy and lactation (Review)

Farzaneh Rassaf,[1,*] Zohreh Shahhosseini,[2]

1. Midwifery Counseling, Mazandaran University of Medical Sciences, Sari, Iran ,
2. Department of Midwifery and Reproductive Health, Mazandaran University of Medical Sciences, Sari, Iran

Introduction: Introduction: Domestic violence means the violent and domineering behavior of a family member against a member or other members of the same family. Nowadays, domestic violence against women has been widely recognized as an important public health problem. Violence in pregnancy can affect a woman's ability to breastfeed in addition to its many consequences for the pregnant woman. The aim of this study was to investigate the factors associated with domestic violence during pregnancy and lactation.

Methods: Materials and Methods: The present study is a domain review study. In this study, 477 articles were covered by e-search by entering the desired keywords in Pubmed, Science Direct, Cochrane Library, SID, Magiran and Irandoc databases from the time period covered by this Banks were acquired by 2021. Finally, 6 studies (3 cross-sections, 1 control case, 1 meta-analysis, 1 cohort) in the period 2001 to 2021 that examined the factors related to domestic violence on pregnant and lactating women were reviewed.

Results: Results: A review of the available articles showed the most common factors influencing domestic violence in pregnancy and lactation, low level of female education (4 studies), low level of spouse education (2 studies), female unemployment (2 studies), alcohol consumption (2 studies) Also in one study, having 3 children or less and visiting a doctor regularly for prenatal care were cited as deterrents to violence during pregnancy. In one of these studies, between husbands' violence against pregnant women with the variables of couples' trust in each other, satisfactory sexual relations ($P < 0.001$) and satisfactory social relations ($P < 0.001$) to and couples' cooperation ($P < 0.001$) There is a significant correlation with each other.

Conclusion: Conclusion: Domestic violence during pregnancy and lactation is an important and significant issue that can be reduced by identifying its risk factors during pregnancy. Therefore, more studies are needed to identify the mechanisms of domestic violence.

Keywords: Keywords: Domestic Violence, Violence, Pregnancy, Breastfeeding

Frequency of (rs34713741)-254C>T polymorphism of Selenoprotein S Gene in Patients with Type 2 Diabetes and Correlation with Selenoprotein S, Glucose and Oxidative Stress Levels (Research Paper)

alireza farrahi,[1,*] Mohsen Firoozrai,[2] Mohammad Hossein Hasani,[3] Ali Asghar Ahmadi,[4] Akram Mehrzad Selakjani,[5] Masoud Tahani,[6]

1. Student, Clinical biochemistry, Medical faculty, Shahrood Azad University, Email: alirezafarrahi95@gmail.com, ORCID iD: 0000-0002-3112-8918.
2. professor, Clinical biochemistry Department, Medical faculty, Shahrood Azad university.
3. Department of Interal medicine, Islamic Azad university, Shahrood Branch, Shahrood, Iran
4. Biochemistry Laboratory, North Reserch Center-pasteur Institue of Iran, Amol, Mazandaran, Iran.
5. Student, Clinical biochemistry, Medical faculty, Shahrood Azad University, ORCID iD: 0000-0001-7938-6759.
6. Student, Clinical biochemistry, Medical faculty, Shahrood Azad university.

Introduction: It is widely accepted that type 2 diabetes is a metabolic disorder, the main characteristic of which is insulin resistance and gradual beta-cell dysfunction. It seems that oxidative stress and low plasma selenoprotein (SelS) levels are associated with an increased risk of diabetes. This study aimed to evaluate rs34713741 polymorphism in a population of diabetics and its relationship with glucose, SelS, and oxidative stress levels.

Methods: This case-control research was performed on 122 patients with type 2 diabetes and 106 healthy individuals from the Diabetes clinics in Tehran (Iran). We determined the levels of glucose, malondialdehyde (MDA), total antioxidant capacity (TAC), and HbA1C and measured lipid profile and SelS levels. The (rs 34713741)-254C<="" p="">

Results: In this study, there was a significant relationship between CT and TT genotype of (rs 34713741)-254C<="" p="">

Conclusion: According to the results of the present study, there was a relationship between rs34713741 polymorphism and type 2 diabetes. In addition, the T allele of the rs34713741 polymorphism had an impact on patients with type 2 diabetes.

Keywords: Polymorphism, rs 34713741, Selenoprotein S, Diabetes Type 2, Oxidative Stress

Frequency of genes involved in irp-1 and irp2 iron acquisition in clinical isolates of Klebsiella pneumoniae (Research Paper)

Fatemeh Bahrami chegeni,[1,*]

1. Razi Herbal Medicine Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran

Introduction: Klebsiella pneumoniae is an opportunistic pathogen of Enterobacteriaceae family that causes sepsis, meningitis, urinary tract infections and soft tissues. Klebsiella pneumoniae produces a number of virulence factors that are involved in pathogenesis. These include: siderophores, O antigens, lipopolysaccharides, and capsules. The irp-1 gene is the number one protein regulator of iron. This gene is responsible for controlling intracellular iron metabolism and can regulate the body's iron homeostasis by regulating histidine. The aim of this study was to evaluate the frequency of irp-1 and irp-2 genes in clinical isolates of Klebsiella pneumoniae.

Methods: In this study, 100 clinical isolates of Klebsiella were collected during 7 months. Samples taken in the laboratory were evaluated differentially and biochemically. Antibiotic susceptibility was assessed by disk diffusion method. DNA extraction was performed by boiling method and genes were identified by specific primers using PCR technique.

Results: Out of 100 samples, 63 samples (63%) were male and 37 samples (37%) were female. Of the total isolates, 83 isolates had resistance, of which the prevalence of irp-1 and irp-2 genes were 73.2% and 53.8%, respectively.

Conclusion: The results of this study show that the prevalence of irp-1 gene is higher than irp2 gene and it was found that there is an increase in resistance to genes involved in iron acquisition in the isolates.

Keywords: Klebsiella pneumoniae, Antibiotic resistance, irp-1, irp2

Frequency of PAH mutations among classic Phenylketon Urea patients in Mazandaran and Golestan Provinces, north of Iran (Research Paper)

Elahe Hosseini,[1] Mohammad Bagher Hashemi-Soteh,[2,*]

1. Novin Genetic diagnostic Laboratory, FarahAbad Boulevard, Sari, Mazandaran, Iran
2. Immunogenetic Research center, Molecular and Cell biology Research center, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.

Introduction: Phenylketonuria (PKU) is the most common aminoacidopathy with an autosomal recessive inheritance pattern. A global PKU prevalence is estimated about 6.002 in 100,000 new born. In Iran, the prevalence of PKU is estimated about 1 in 4,698 and it shows an increasing trend from north (0.0015%) to south (0.02%) of the country. Untreated PKU causes mental retardation, microcephaly and seizure. PAH gene mutations located at chromosome 12q23 are responsible for the classical type of this disease. The spectrum of PAH mutations is varied in different ethnicities and different parts. The aim of this study was to investigate the frequency of PAH mutation in Mazandaran province, which could be useful for genetic counseling and prenatal diagnosis.

Methods: A total of 66 individuals from 33 families from two provinces (9 family from Golestan and 24 family from Mazandaran) from north of Iran participated in this study. After genomic DNA extraction, PAH gene analysis was carried out using DNA sequencing of both coding and non-coding regions by ABI 3130XL genetic analyzer.

Results: 26 different mutations were identified in PAH gene in this study. Four mutations including IVS10-11 (c.1066-11G>A), c.727C>T (p.Arg243X), c.898G>T (p.Ala300Ser) and c.601C>T (p.His201Tyr) were the most common mutations with 37.48% frequency in Mazandaran province. Most frequent mutations in Golestan province were IVSI0-11 (c.1066-11G>A), c.722delG (p.Arg241fs), c.842C>T (p.Pro281Leu) and IVSII+5 (G>A) with frequency 58.57 % respectively

Conclusion: The results from present study verify heterogeneity of the PAH gene and may help to diagnosis tests for carrier detection and prenatal diagnosis of the PKU disease in Iranian population.

Keywords: Phenylketonuria; PAH gene; Iran; Mazandaran; Golestan; Mutation detection

Frequency Of PGP and MRPA genes in clinical isolates of leishmaniasis
(Research Paper)

maede parishan,[1,*]

1.

Introduction: Leishmaniasis is one of the most common infectious diseases in tropical and subtropical areas in the world which is reporting from Iran and more than 90 countries all around the world. Generally primary treatment of leishmaniasis depends mainly on pentavalent antimonies including Glucantime and Pentostam and resistance to these compounds has been reported in recent years. Failure to treatment and decrease in effectiveness of Glucantime has been reported from Iran. Resistance to antimonial compounds may occur due to several mechanisms and several genes related to the resistance are detected, including efflux pomp genes MRPA and mdr1 that code ABC transporters which efflux drugs from the cell membrane or sequester metal-thiol conjugates. The aim of this study is to detect mdr1 and MRPA genes in clinical isolates of Leishmania promastigotes.

Methods: In this study, during a period of 24 months, direct samples were taken from skin lesions of patients who referred to Center for Research and Training in Skin Diseases and Leprosy. Smears were prepared from the lesions and stained with Giemsa and directly examined for the presence of Leishmania amastigotes under the light microscope. Part of discharge was inoculated into biphasic culture media NNN (consisted of Agar, Rabbit's blood & liquid phase RPMI) or NNNN (consisted of Agar, Rabbit's blood, liquid phase Lockes) and after incubation were examined for the presence of promastigotes. Also for detection of Leishmania species, part of the discharge was transferred to vials containing sterile PBS for PCR test. DNA extraction was done by phenol- chloroform procedure from amastigotes of lesions or from promastigotes which were grown in liquid media RPMI enriched with 10 % FBS. The species of Leishmania (L. tropica or L. major) were detected by PCR using specific primer for ITS region. Then frequency of efflux genes MRPA and mdr1 was determined by using PCR method. For this purpose, specific primers targeted conserved regions were designed by using softwares. During the set up procedure, different concentrations of reaction mixture and temperatures were examined.

Results: In total 40 cutaneous leishmaniasis patients were included, from whom 40 strians of Leishmania were isolated. Twenty samples were used during set up procedure of PCRs and the remaining 20 isolates were used for molecular characterization of efflux pomp genes. From 20 isolates, 9 samples (45%) were positive in stained smear, 9 samples (45%) were positive in 3N/4N culture and 16 samples (80%) were positive in PCR. By PCR, 6

samples (30%) were characterized as L. major, 10 samples (50%) as L. tropica and 4 samples (20%) were unidentified. From 20 isolates, 19 samples (95%) were mdr1 positive, 10 samples (50%) were MRPA positive and 10 samples (50%) had both genes. Among MRPA positive samples, 4 were L. tropica and 5 were L. major, while among MDR positive samples, 10 were L. tropica and 5 were L. major

Conclusion: In this study, ABC transporter genes particularly mdr1, which previously was identified in experimentally induced resistance strains of Leishmania spp., were successfully identified in clinical isolates of Leishmania causing cutaneos leishmaniasis. Confirmation of the possible role of these genes in drug resistance requires further study.

Keywords: Cutaneous leishmaniasis; Drug resistance; Efflux pomps; Antimonial compounds; L. major; L. tropica

Frequency of polymorphism (rs28665122)-105 G>A in selenoprotein S gene among patients with type 2 diabetes and its correlation with selenoprotein S and glucose levels and oxidative stress status

(Research Paper)

Akram Mehrzad Selakjani,[1,*] Mohsen Firoozray,[2] Mohammad Hossein Hasani,[3] Sahar Moghbelinejad,[4] Alireza Farrahi,[5] Masoud Tahani,[6]

1. Student, Clinical biochemistry, Medical faculty, Shahrood Azad university, Email: akram919mehrzad@yahoo.com, ORCID iD: 0000-0001-7938-6759
2. professor, Clinical biochemistry Department, Medical faculty, Shahrood Azad university.
3. Department of Interal medicine, Islamic Azad university, Shahrood Branch, Shahrood, Iran
4. Cellular and Molecular Research Center, Qazvin university of medical sciences, Qazvin, Iran.
5. Student, Clinical biochemistry, Medical faculty, Shahrood Azad university, ORCID iD: 0000-0002-3112-8918.
6. Student, Clinical biochemistry, Medical faculty, Shahrood Azad university.

Introduction: Type 2 diabetes (T2D) is a type of metabolic disorder characterized by high blood glucose levels in conditions of insulin resistance and relative insulin deficiency. Oxidative stress can play a role in the development and progression of this disease. Selenoprotein S is an essential antioxidant protein. Accordingly, the purpose of this study was to evaluate the role of selenoprotein S gene (rs28665122)-105 G>A polymorphism in T2D.

Methods: The present case-control study was conducted on 115 T2D patients and 109 healthy individuals from the Diabetes clinics in Tehran (Iran). After collecting venous blood samples, the measured parameters included glucose level, malondialdehyde (MDA) content, total antioxidant capacity (TAC), and HbA1c level. Serum selenoprotein S (SEPS1) level and lipid profile were measured as well. The SEPS1 gene promoter polymorphism (rs28665122)-105 G>A was analyzed by RFLP technique and the correlation between genotype and serum parameters was also evaluated.

Results: The mean total cholesterol concentration was not significantly different between the patient and healthy groups; however, the other studied biochemical parameters showed a significant difference between the two groups. It was also revealed that the subjects with GA and AA genotypes at rs28665122-105 G>A with OR = 0.985 and OR = 4.044 had a higher risk of diabetes than the normal genotype, respectively. Among the serum parameters studied, only blood glucose concentrations, HbA1c and HDL-C had significant correlations with different genotypes.

Conclusion: The results of this study indicate the correlation between rs28665122 polymorphism and T2D and also the effect of allele A of this polymorphism on T2D incidence.

Keywords: polymorphism, rs28665122, selenoprotein S, type 2 diabetes, oxidative stress

Functional mechanism of miR-1270 in cancer development (Review)

Anita Alizadeh,[1,*]

1. M.SC. student of Genetics, Department of Biology, Higher Education Institute of Rab-Rashid, Tabriz, Iran

Introduction: Cancer is one of the most leading causes of death in the worldwide. Common cancer treatment methods such as surgery, chemotherapy and hormone therapy are limited to the early stages of cancer development. Therefore, it is necessary to develop novel therapeutic methods which are more beneficial and have fewer complications. Furthermore, discovering new prognostic and diagnostic biomarkers for early detection of cancer is very helpful to more effective treatment. microRNAs (miRNAs) are categorized as short non coding RNAs which have 22 nucleotides in length and highly conserved through out evolution. They are considered one of the important regulatory mechanisms of gene expression by interaction with 3′ untranslated regions (3′-UTR) of mRNAs and subsequently lead to mRNA translation suppressing or degradation of mRNA. According to miRNA target databases, one miRNA may regulate several mRNAs and its targets whereas One mRNA may be targeted by various miRNAs. Among numerous functional miRNAs which may be associated with human cancers, miR-1270 have been shown that has pivotal role in cancer cell development and aberrant expression of this miRNA have been illustrated in different types of cancer.

Methods: In this review data were obtained from searching the scientific resources including PubMed, google scholar, science direct and library resources and related books, For aim to know miR-1270 regulatory mechanism and its interaction with other genes and signaling pathways in cancer development.

Results: Studies have shown that miR-1270 has high expression in several cancer such as thyroid, osteosarcoma and lung cancer and upregulated expression of it may has interaction with signaling pathways including NF-kappaB and wnt signaling pathways. Moreover miR-1270 can be regulated by circular RNAs (circRNAs) such as circRNA Cdr1as, circ sox4 and circ0001247 also with such lncRNAs including SNHG8, GLIDR in various types of cancer furthermore it has been demonstrated that miR-1270 may interact with interferon-alpha1 and its nature antisense mRNAs to modulate homeostasis in human cells.

Conclusion: It was concluded that miR-1270 mainly functions as an oncogene in different cancers, there were also significant association between miR-1270 and other ncRNAs in tumor cells. Moreover miR-1270 has a critical

role during tumor progression using the regulation of signaling pathways and may act as a novel biomarker in cancer diagnosis and treatment.

Keywords: Non coding RNA, MicroRNA, MiR-1270, Cancer, Biomarker.

gaining insight into diabetogenicity of SARSCoVII and other possibilities (Review)

Kimia Sagharichi ,[1] Saman Hakimian,[2] Shaghayegh Yazdani,[3,*]

1. Department of microbiology, Faculty of Advanced Science and Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran
2. M.sc student of Pathogenic Microbes Islamic Azad universtity, Central Tehran Branch, Tehran, Iran
3. Department of microbiology, Faculty of Advanced Science and Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

Introduction: Coronavirus disease 19 (covid19), caused by the seventh coronavirus, SARScoVII, was first reported in Wuhan, Hubei province, China, in December 2019 and spreading swiftly all around the globe, resulting in protected public health emergency in our time. One study showed that SARScoVII binds to ACEII, an essential receptor for viral entry and Renin-angiotensin-aldosterone system down regulator, with 10-20 times higher affinity compared to SARS-CoV. However, it has been seen that it is not only not inhibited by ACE-inhibitors or angiotensin blockers but also is up-regulated with their use. As both viruses have a homology of 70% in terms of genome, structure, and even pathogenicity, considering the effects of the first novel virus can help to distinguish the latter.

Methods: A recent study showed that CD4+ and CD8+ decreased in covid19 patients resulting in cytokine and chemokine storm. Additionally, new data indicates that 20-50% of patients with a positive PCR test for SARScoVII have chronic diabetes, the second most common disease associated with SARScoVII, affecting all age groups, mostly 47-59-year-old folks and even the comparison of pre-prandial and post-prandial glucose levels revealed 29.4% and 64.5% above target levels, respectively and at least one hypoglycemic event occurrence. In another study on a one-year-old Hispanic male with no comorbidities presenting anorexia, polydipsia, a 10-pound weight loss over three weeks with an initial blood glucose level of 470 mg/dL and HbA1c of about 14.8%, and positive results from nasal swab test using Thermo fisher essay on the admission day without showing any symptoms of fever, cough and respiratory. The second test was taken on the third day of hospitalization using the BDmax assay and turned positive. Markers of T1DM such as islet antigen2 antibodies and glutamic acid decarboxylase antibody titers were grossly abnormal. After the patient's discharge with oral potassium and 2000 IU vitamin D and lockdown and DKA protocol, he was seen one day, one week, three weeks afterward, and DM was well-controlled.

Results: Respiratory: the severity of covid19-related respiratory diseases varies significantly from mild requiring minimal oxygen support with a nasal

cannula to acute hypoxemic respiratory failure requiring ventilation. In 80% of cases, the disease is only limited to the upper respiratory tract, but in the remaining 20%, pulmonary infiltrates indicating alveolar viral invasions have been witnessed. Hematologic system: covid19 has affected the hematologic system in the forms of lymphopenia, especially in severe cases. Inflammatory indices such as lactate dehydrogenase, C-reactive proteins, and IL-6 or even hyperprocalcitonin and hyper-ferritin may emerge as poor prognosis identification.

Conclusion: Patients with covid19 are also at a higher risk of venous thromboembolic (VTE) diseases because elevated serum fibrinogen and D-dimer levels, producing while the body is forming or breaking clots, are common coagulopathy see in hospitalized covid19 patients. Increased serum D-dimer levels can demonstrate increased mortality rate amongst covid19 patients; in one cohort study examining the rate of thromboembolic events in 184 ICU patients, all standard receiving dosage of VTE prophylaxis showed the thromboembolic event incidence of 31%. Cardiovascular system: between 5%-25% of hospitalized covid19 patients will have an incidence of myocardial involvement, as well as what has witnessed in the autopsy of covid19 patients, manifested by infractions, heart failure, and dysrhythmias due to increased metabolic demands and procoagulatory activity. Also, higher serum troponin levels, described as an indicator of cardiac injuries and hypoxia, can be seen in many covid19 hospitalized patients. Neurologic system: neurologic manifestations have been reported in more than one-third of covid19 patients. The potential neurologic damage includes direct viral neuron damages, excessive pro-inflammatory responses, and unintended host immune responses after the acute phase. The prevalence of hypogeusia and hyposmia suggest viral invasion of the olfactory nervous system via the olfactory bulb.

Keywords: SAESCovII, Diabetes, Acute respiratory syndrome, Novel coronavirus disease, Autoimmune disease

Generation of electricity from methanogens using food waste (Research Paper)

Ali Khanifar,[1,*] Rezvan Cheraghale,[2]

1. kurdisstan universityof medical sciences
2. Islamica Azad university of dezful

Introduction: According to the FAO: 870 million people, equivalent to one-eighth of the world's population, do not have enough food to eat. In the UK, food waste is 10 million tonnes. In German restaurants, if you spend too much, you will be fined according to the national code. In South Korea, restaurants calculate the exact average customer food and price it based on the amount of food.Chinese restaurants have semi-press dishes for their customers. In the United States alone, 40 percent of the food produced is discarded each year. The highest level of food waste is for Saudi Arabia. Every Saudi citizen throws away about 427 kilograms of food a year.Among developed countries, the United States and Denmark have the highest rates of food loss. Situation in Iran:Iran's food loss rate is 2.7% of the total world. The amount of food waste in Iran is equal to 10 European countries. Food waste in Iran is equivalent to 35 million tons per year and in the European Union with 27 member countries is about 90 million tons. Food loss in Iran is equivalent to the annual food of 15 million people. The Urban Scientific-Economic Association of Iran has estimated the value of 35 million discarded foods at nearly 38,000 billion tomans. 100 million tons of agricultural products are produced annually in Iran and 30% of it is wasted before consumption for various reasons. To prevent this waste of food, a practical solution is needed. Since culture-building takes time, the only option now is to use food waste to convert it to methane and then generate electricity. In fact, we turn it into a positive factor.In this article, we will discuss how to produce methane as well as electricity from methane.

Methods: Waste produced in the kitchen, including vegetables, fruits, cooked and uncooked foods, and dairy products, has been used in anaerobic digestion tests. Waste was separated from materials such as bone, soil, sand and soap, detergents and polymeric materials so that all materials used were organic and biodegradable. This waste was crushed by a meat grinder or mixer and cut into small pieces. Became. The crushed samples are then poured into steel reactors designed for anaerobic digestion. Heated water is also used to regulate the reactor temperature. Because the anaerobic fermentation process is time consuming, microbial filters are installed for the exhaust pipes, the gases of which are mainly methane, and are used to prevent methanogens from escaping to other parts. In fact, after preparing methane, they are put in the concentrationprocess and then sent to the factory to generate electricity.

Results: We conclude that the process of producing methane from methanogens is time consuming but more economical than current methods and has a high efficiency. Also, the use of methane produces high electricity and is in fact a kind of culture of society towards the use of renewable fuels.

Conclusion: Given the statistics mentioned about food waste in Iran and the lack of an alternative solution, the existence of such a solution could be a potential alternative. This method will also be effective with the tendency of the society towards the use of renewable fuels.

Keywords: Methane- Methanogens-Food leftovers

Genetic assessments in dentigerous cyst (Review)

Shirin Saravani,[1,*] Hamideh Kadeh,[2]

1. Oral & Dental Disease Research Center, Department of Oral & Maxillofacial Pathology, Zahedan University of Medical Science, Zahedan, Iran
2. Oral & Dental Disease Research Center, Department of Oral & Maxillofacial Pathology, Zahedan University of Medical Science, Zahedan, Iran

Introduction: Dentigerous cyst (DC) is the most common odontogenic cyst, which results from the accumulation of fluid between the reduced enamel epithelium and the crown of the tooth. The role of genetic changes in the pathogenesis of this cyst has not been precisely elucidated. The P53 mutation was seen in codon 237 and the FHIT LOH mutation was seen in 10% of dentigerous cysts. In addition, mutation of PTCH gene has been identified as Loss of heterozygosity for D95287 and D95180 markers in 50% of cases of dentigrous cysts. LOXL4 mRNA expression was also seen in dentigerous cysts but was 3.7 times lower than in odontogenic keratocysts. 1qht chromosome polymorphism has also been observed in dentigerous cysts. Evaluation of genetic aberrant in dentigerous cysts has been done in few studies and most studies have examined the gene expression of different proteins by immunohistochemistry. These studies showed immunohistochemical expression of sonic hedgehog signaling pathway markers, Ki-67, CD138, RANK/RANKL, OPG, clusterin, P63, PCNA, elafin, Extracellular Matrix Metaloproteinase inducer in dentigerous cysts. In this study, we try to review the research done on genetic aberrant and expression of different proteins on dentigerous cysts.

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Keywords: Dentigerous Cyst, genes, Polymerase Chain Reaction, Immunohistochemistry

Genetic mutations and causative agents and prevention (Review)

Mahya Badbarouni,[1,*]

1. Azad university of Dezful

Introduction: Cell division is the process by which a mother cell transforms into two or more other cells. An average of about a trillion cell divisions occur daily. O carries all the genetic code and information. Genes are made by placing four nucleotides (DNA-making molecules) of adenine (A), thymine (T), guanine (G), and cytosine (C) in the DNA molecule sequence. In fact, a specific sequence of placement of these four molecules is called a gene. Each gene, like a manual, maintains the sequence of placement of specific codes that the cell can use to make the proteins it needs. Make. A gene mutation is a permanent change in the sequence and order of the DNA codes that make up a gene, so that that sequence is different from what is found in other people. Mutations come in different sizes, they can affect anywhere in a gene. These changes can affect anything from a single nucleotide in DNA (base pair) to a large fragment of a chromosome that contains multiple genes. Each cell division involves steps that may lead to errors in the arrangement of proteins. DNA is possible. In any of the activities, such as the transcription process, replication or recombination of chromosomes, there is a possibility of errors in genetic information. And one of the rare cases of spontaneous change is DNA, which is called a mutation. The parent is inherited and is present in all cells of the body throughout a person's life. These mutations are also called germline mutations because they are present in sperm and egg cells, also called germ cells. When an egg and a sperm merge, the resulting fertilized egg cell receives DNA from both parents. If this DNA has a mutation, the offspring of that egg will have that mutation in each of its cells. Acquired (or somatic) mutations that sometimes occur throughout a person's life and are present only in certain cells, not in all cells of the body. . These changes can be caused by environmental factors such as the sun's ultraviolet radiation, or if an error occurs during DNA replication on its own, that is, during cell division. Acquired mutations in somatic or somatic cells (cells other than sperm and eggs) are not passed on to the next generation. External factors such as physical atoms such as atomic and cosmic rays, ultraviolet rays, etc., or chemical agents such as nitrogen and mustard gas, acridine dyes, benzoprene, and many chemical compounds such as chemical compounds such as alkylating agents, game analogs, anti Biotics are mutants that can cause damage to genetic material in any particular way. Some mutations are permanent and some are temporary, also called conditional mutations, meaning that as long as the conditions, causes, and causes of the mutation exist. The mutated phenotype appears and remains and disappears as the conditions or causes of the mutated phenotype disappear. Monet is a reactive species of oxygen, nitrate and nitrite, some metals, drugs and those

substances that existed in human nature (household chemicals, additives and flavors and preservatives).

Methods: by review and study other articles

Results: Antioxidants - An important group of compounds that prevent exposure to carcinogens. And they can help protect against all kinds of hostile chemicals. Examples of antioxidants are vitamins A, C and E, beta-carotene and flavonoids. These substances are found in very large numbers in fruits and vegetables as well as in green tea, it is important to try to avoid UV rays and smoke cigarettet and drugs and alcohol.By modifying your lifestyle and avoiding harmful chemicals and radiation, gene mutations can be largely prevented.

Conclusion: Cells are growing and dividing every day, and humans are exposed to a variety of destructive substances and compounds and various rays that cause mutations, ie changes in a person's DNA. Some mutations are ineffective and some cause disease and defects. Most mutations are common. They can lead to cancer, which can be prevented by following simple steps.

Keywords: Genetic mutation.Gen.Cell division.Prevention

Genetic polymorphism of metabolic enzymes of Leishmania spp. parasites isolated from different clinical types of cutaneous leishmaniasis patients (Research Paper)

Mahmoud Nateghi Rostami,[1,*] Mansoureh Hosseini,[2] Fatemeh Darzi,[3]

1. Department of Parasitology, Pasteur Institute of Iran
2. Department of Microbiology, Faculty of Advanced Sciences, Islamic Azad University of Medical Sciences
3. Department of Parasitology, Pasteur Institute of Iran

Introduction: Cutaneous leishmaniasis (CL), mainly caused by Leishmania major and L. tropica species, is a geographically extensive disease with diverse clinical manifestations. The most common CL lesion is a self-healing typical ulcer, leaving a scar, however, lesions can be highly polymorphic, and frequently appear as atypical lesions described as ‘eczematoid’, ‘chancriform’, ‘erysipeloid’, ‘zosteriform’, ‘lupoid’, ‘sprotrichoid’, etc. Parasite genetic diversity is proposed to be one of the factors affecting the characteristics of clinical lesions in CL. This study aim to explore potential association of genetic diversity of enzymatic markers with clinical type of CL.

Methods: Specific genes encoding metabolic enzymes, mainly used for MLEE, including isocitrate dehydrogenase (icd), mannose phosphate isomerase (mpi), glucose-6-phosphate dehydrogenase (g6pd), fumarate hydratase (fh), 6-phosphogluconate dehydrogenase (6pgd) and aspartate aminotransferase (asat) were selected. We applied a PCR-sequencing and multilocus sequence typing (MLST) analysis to explore genetic variations of Leishmania strains isolated from atypical vs. typical CL patients from Iran using BioEdit, Mega7, DnaSP and MLSTest softwares.

Results: A total of 41 isolates of L. major (28/41) and L. tropica (13/41) from 21 (51.2%) atypical CL and 20 (48.8%) typical CL cases were included. A set of additional sequences of 41 strains of 17 species of Leishmania were retrieved from databases. Different SNP variations were detected and the highest rate of heterozygous sites was found in g6pd and 6pgd genes (6 sites) for L. tropica and in asat and 6pgd genes (7 sites) for L. major strains. All strains were clustered into 58 unique sequence types (STs) including 17 STs related to 41 strains of Leishmania of this study. Concatenated tree clustered all strains in 6 main clades (A to F) including L. major (clade D) and L. tropica (clade B) strains. All of the STs were related in clonal complexes by using eBURST with the prediction of founder genotypes.

Conclusion: A high rate of genetic variations and heterozygocity was evident in L. tropica and L. major strains; nevertheless, there was no significant

difference in the diversity of Leishmania strains between typical CL and atypical CL groups. This study represents the first successful application of MLST approach to L. tropica and L. major strains in Iran.

Keywords: Cutaneous leishmaniasis; Genetic diversity; Iran; Leishmania; MLST

Germ cell differentiation of mouse embryonic stem cells can be influenced by the culture medium (Research Paper)

azam soleimani,[1,*] Nehleh Zareifard,[2] soghra bahmanpour,[3]

1. Shiraz University of Medical Sciences, Shiraz, Iran
2. Shiraz University of Medical Sciences, Shiraz, Iran
3. Shiraz University of Medical Sciences, Shiraz, Iran

Introduction: Because embryonic stem cells (ES) can develop into germ cells, optimizing culture conditions for differentiation of ES is highly desirable. In practice, ES cell differentiation protocols for generating germ cell-like cells use either traditional media such as Dulbecco's modified Eagle's medium (DMEM or basal ES cell media, such as knockout Dulbecco's modified Eagle's medium (KODMEM). We have found no standardized culture medium for induction of germ cell differentiation from ES cells despite the fact that the effect of culture medium on development of gonadal germ cells in vitro has been investigated extensively. We compared two commonly used commercial media, high glucose DMEM and KO-DMEM, and assessed the germ cell differentiation from mouse ES cells by evaluating germ cell expression using EB or monolayer culture systems.

Methods: The mouse ES cell line R1(XY) was cultured on mitomycin C treated mouse embryonic fibroblast in KO-DMEM containing 15% ES qualified FBS, 1% penicillin/streptomycin, 2 mM L-glutamine, 0.1 mM nonessential amino acids, 0.1 mM β-mercaptoethanol and 1000 U/ml LIF. Half of the medium was replaced each day and the cells were passaged every second day. Germ cell differentiation was induced in mouse ES cells under four experimental conditions: EB/Dulbecco's modified Eagle's medium (EB/DMEM), EB/knockout Dulbecco's modified Eagle's medium (EB/KO-DMEM), monolayer/Dulbecco's modified Eagle's medium (monolayer/DMEM), and monolayer/knockout Dulbecco's modified Eagle's medium (monolayer/KO-DMEM). After incubation for 6 days, quantitative real-time polymerase chain reaction (qRT-PCR) was used to assess expression of the germ cell markers, Mvh, Oct4, Rec8, Scp1, Scp3 and Stra8. Also, Oct4 and Mvh expressions at the protein level were assessed using immunocytochemistry; we evaluated alkaline phosphatase activity in addition to cell number and viability. Cell phenotypes were checked every day, using an inverted microscope (Olympus). Their growth was evaluated using trypsin/EDTA (0.05%) digestion for about 5 min to form a single cell suspension of the EBs. EB volumes and the dark areas at the center of each EB were estimated by measuring the mean value of the four diameters of each EB using the formula r3 π4/3, where r = radius.

Results: Germ cell-specific marker expression was increased significantly in cells differentiated in KO-DMEM for both EB and monolayer protocols; the highest level was in cultures using the EB protocol. The highest cell proliferation rate was observed using the monolayer/KO-DMEM protocol and the lowest using the EB/DMEM protocol. Generally, KO-DMEM exhibited the greatest impact on germ cell differentiation and cell proliferation.

Conclusion: We found that KO-DMEM is suitable for both monolayer and EB differentiation conditions. KODMEM is the superior medium for male and female germ cell differentiation. We found that the EB protocol, in the presence of KODMEM, is more efficient for promoting the expression of germ cell markers than the monolayer condition in the same medium. we speculate that this biomimicry might be reinforced in KO-DMEM. We also demonstrated that the volume of the dark area of EBs increased and number of viable cells decreased when EBs were cultured in DMEM. Commercial culture media and serum supplements contain different amounts of reactive oxygen species (ROS). Therefore, the lower number of viable cells and larger dark areas seen after using the traditional DMEM protocol could be due to increased ROS production. On the other hand, it has been shown that loss of Oct4 in PGCs was correlated with apoptosis. Our findings show that Oct4 expression by cells differentiated using DMEM was extremely low, which suggests that our results might explain the lower cell viability in traditional media. Unknown components in proprietary media might be responsible for reduction in cell numbers in the outcome of PGC differentiation. We found a higher rate of germ cell differentiation in the ES cells cultured in KO-DMEM compared to those incubated in DMEM both in the presence or absence of BMP4. Our findings are consistent with earlier reports that optimization of culture conditions and appropriate choice of medium are critical for each differentiation protocol.

Keywords: culture medium, embryonic stem cell, germ cell, monolayer culture

Gradient Scaffolds in Tissue Engineering (Review)

Elham Ansari,[1] Ashrafalsadat Hatamian-Zarmi,[2] Zahra-Beagom Mokhtari-Hosseini,[3,*] Mohammad Naji,[4] Soheil Kianirad,[5] Zahra Kazemizadeh,[6]

1. Department of Life Sciences Engineering, Faculty of New Sciences and Technologies, University of Tehran
2. Department of Life Sciences Engineering, Faculty of New Sciences and Technologies, University of Tehran
3. Department of Chemical Engineering, Faculty of Petroleum & Petrochemical Engineering, Hakim Sabzevari University
4. Urology and Nephrology Research Center, Shahid Beheshti University of Medical Sciences
5. Department of Life Sciences Engineering, Faculty of New Sciences and Technologies, University of Tehran
6. Department of Chemical Engineering, Faculty of Petroleum & Petrochemical Engineering, Hakim Sabzevari University

Introduction: Tissue engineering and regenerative medicine are new strategies in tissue development with the aim of replacing, repairing, or improving biological activity of tissues by manipulation of cells through their extracellular environment. Current approach in tissue engineering involves the development of natural tissues' features by designing biomimetic scaffolds. Scaffolds are engineered structures that, as extracellular matrix (ECM), plays the role of 'home' to cells. One approach to mimic ECM is the use of gradient scaffolds. Gradient scaffolds have gradual or abrupt transitions in one or some of their properties. These changes can be seen in mechanical properties, cross-linking density and meshing size, porosity, composition, and biochemical properties in the forms of temporal or spatial gradients. Cells are constantly exposed to temporal or spatial gradient of physical or chemical signals. Gradient scaffolds utilize these gradients to regulate cellular functions. Some advantages of gradient scaffolds are elimination of high local stresses in the interface of different scaffold layers, prevention of delamination, effective signal transmission and regulation of cellular behavior, and efficient ECM simulation.

Methods: In this review, information collected from relevant published articles were used to present a summary of different forms of gradient scaffolds, recent advances of gradient scaffolds fabrication, and their application in tissue engineering.

Results: Gradient scaffolds are mainly classified as physical and chemical gradients. Physical gradients include gradual changes in structure, porosity, composition, stiffness, fiber alignment and architecture that affect the cellular behaviors. Physical gradients are mostly used in soft-to-hard interface

scaffolds. By changing the material type or manipulating their feature, it is possible to create multidimensional scaffolds to treat both cartilage and bone layers, bone and muscle layers and so on. Chemical gradients are defined as gradients in morphogens, proteins, drugs, bioactive substances, or cell type that provide necessary biochemical signals to guide tissue formation. The absolute concentration or gradient slope are important factors that should be considered prior to fabrication of these scaffolds, as cells respond differently depending on these factors. Chemical gradients can provide different metabolically needs of various cell types or adjacent tissues and thus mimicking the physiological environment more efficiently. Combination of physical and chemical gradients will further increase the accuracy of tissue engineering outcome. For example, smart drug delivery such as drug release in a particular manner, and sustained release of drugs or bioactive factors can be achieved by designing scaffolds with gradual changes in physical properties of scaffold and embedment of various substances. There are various fabrication methods for gradient scaffolds such as additive manufacturing, component redistribution, controlled phase changes and post-modification, which are further divided into subcategories. The ideal gradient scaffold should have continuous and smooth transition which some methods such as layering are unable to do so. Some methods such as electric attraction and magnetic attraction use external forces to form gradient changes. Also, methods such as electrospinning and 3D printing can form a range of gradients. But due to the high precision required for gradient formation and its unique complexity, mass production of these scaffolds has not yet been achieved.

Conclusion: By mimicking the extracellular matrix, gradient scaffolds provide more appropriate environment for cellular behavior regulation and tissue engineering. These scaffolds utilize various types of gradients such as gradual transitions in cell type, morphogens, scaffold structure or porosity that make them great option for simulation of soft-to-hard tissue interface. However, one of the main challenges of gradient scaffolds is their fabrication methods. By optimizing fabrication methods, with the aim of development of continuous and smooth gradients, these scaffolds will be able to further mimic the extracellular environment and be of valid choice in tissue engineering, cancer studies and drug discovery.

Keywords: Gradient scaffold, tissue engineering, soft-to-hard tissue interface, gradual transition

Green Tea Epigallocatechin Gallate Enhances In Vitro Immunomodulatory and Beta Cell Protective Functions in Streptozotocin-Induced Diabetic Mice Model with Bone-marrow-Derived Mesenchymal Stem Cells (Research Paper)

Fatemeh Ahmadzadeh,[1] Saeid AbedianKenari,[2,*]

1. Immunogenetics Research center, Department of immunology, Faculty of Medicine,Mazandaran university of medical sciences, sari, Mazandaran, IRAN
2. Immunogenetics Research center, Department of immunology, Faculty of Medicine,Mazandaran university of medical sciences, sari, Mazandaran, IRAN

Introduction: Mesenchymal stem cells (MSC) are judged by their ability as an immunomodulator and their potential to regenerate the insulin secreting cells in type 1 diabetes (T1D). However, some experimental results indicate that the high glucose concentration or diabetic environment suppresses some crucial proteins and increases senescence in stem cells. Regarding antioxidative and immunosuppression characteristics of epigallocatechin-3-gallate (EGCG), the present study investigated the feasibility of using EGCG, along with MSCs, to improve regeneration in pancreatic beta cell line (bTC3) and modulation in immune responses.

Methods: MSCs were extracted from bone marrow of normal mice and cultured. Diabetes was induced in the mice by administration of multiple low-doses of streptozotocin. Splenocytes were prepared from normal and diabetic mice. Proliferation, cytokine production and insulin secretion assays were performed in coculture experiments.

Results: Comparing with other groups, significant improvement in viability as well as insulin secretion of treated bTC3 cells was observed in the MSC+ EGCG group. The EGCG and MSCs treatment more efficiently inhibited splenocyte proliferative response to trigger. Decreased production of IFN-Ɣ as a proinflammatory cytokine and increased secretion of IL-4 as a regulatory cytokine by stimulated splenocytes were also shown in response to stimulant.

Conclusion: On the whole, it seems that natural anti-inflammatory products and stem cell treatment cross-effect may provide a new horizon for T1D cell therapy and islet transplantation in the future.

Keywords: Mesenchymal Stem Cell, Epigallocatechin gallate, Type 1 diabetes

Gut - brain communication and effects of microbial short chain fatty on Alzheimer disease (Review)

Maryam Mazaheri,[1,*]

1. Department of Physiology, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran

Introduction: Alzheimer's disease (AD) is a neurodegenerative disorder and one of the most common causes of forgetfulness in the old ages. Short-chain fatty acids (SCFAs); the main metabolites produced by bacterial fermentation in the gastrointestinal tract are supposed to play key roles in AD pathogenesis. This Review summarizes the potential effects of these SCFAs on β-amyloid (Aß) mediated processes in AD pathogenesis.

Methods: We searched literature available with acute key words" Alzheimer disease" Gut-Microbiota" Short chain fatty acids" in PubMed and Web of science, Scopus. All articles were published from 2017 to 2021 and have ethical considerations.

Results: It is estimated that approximately 66 million people will suffer from Alzheimer's in 2030 and up from 115 million in 2050. Beta-amyloid (Aß) is thought that initiate neuronal inflammatory processes, which is a hallmark of AD. Amyloid deposition occurs by the accumulation of Aß produced from amyloid precursor protein (APP). This accumulation occurs 15 to 20 years before the onset of AD. Human intestinal microbes, as one of the largest human microbial reservoirs, contain 1014 of the at least 1000 microbial species and (density are above 10 to the power of 12 per mile) that differ in diversity and stability among different individuals. William James and Carl Lange initially explained that there is a two-way connection between the central nervous system and the microbiota, the microbial population in the gastrointestinal tract of organisms, which is traditionally referred to gastric flora and its function is beneficial for host health, which includes: maintaining the integrity of the intestinal barrier, inhibiting the binding of pathogens to the intestinal surface, synthesizing vitamin K, energy salvaging of foods not absorbed by the production of short-chain fatty acids (SCFA). Gut microbiota plays a crucial role in host's health and disease. Gut microbiota can influence human brain function and behavior. By any alterations in balance of intestinal bacteria (dysbiosis) onset of neurodegenerative process such as AD is inevitable. Gut microbiota is recently considered as a potential factor in AD. Although, their effects on AD pathology remain uncertain. Microbiota metabolites such as SCFA that is fermented from dietary fibers may alter the brain tissue and causes neurodegenerative disorder. Due to hemostasis of hosts, it received most attention in various studies. In this review results showed that the level of SCFAs and subsequently, cognitive ability was

decreased due to amyloid deposition. Although, the pathways through which SCFAs may influence psychological functioning, including affective and cognitive processes have not been fully yet elucidated especially in humans. Germ-free (GF) AD mice exhibit a substantially reduced Aß plaque load and markedly reduced SCFA plasma concentrations; conversely, SCFA supplementation to GF AD mice was sufficient to increase the Aß plaque load to levels of conventionally colonized animals. While Aß generation was only mildly affected, we observed strong microglial activation and upregulation of ApoE upon the SCFA supplementation. Taken together, our results demonstrate that microbiota-derived SCFA are the key mediators along the gut-brain axis resulting in increased microglial activation, ApoE upregulation and Aß deposition. Our studies supports the hypothesis that intestinal microbiota may capable protect against AD, in part, by potently inhibiting the generation of select SCFAs, which interfere with the formation of toxic Aß aggregation.

Conclusion: This review supports this fact that gut microbiota may help protect against AD progression by generation of SCFAs, which this process interfere with the formation and aggregation of insoluble Aß plaques. Our review highlights how lastly, the development of treatments approachs based on SCFAs can be useful and effective in central nervous system (CNS) disease.

Keywords: Neurodegenerative disorder, Alzheimer disease, Gut microbiota, Bacterial metabolites, Short chain fa

H19/hsa-miR-324-3p/THY1 CeRNA axis affects gastric cancer development by regulating "Integrin beta-2" signaling pathway: bioinformatics gene expression profiling and RNA interaction analysis

(Research Paper)

Golnar Chapnevis,[1] Mohammad Rezaei,[2] Mansoureh Azadeh,[3,*]

1. Zist Fanavari Novin Biotechnology Institute, Isfahan, Iran
2. Zist Fanavari Novin Biotechnology Institute, Isfahan, Iran
3. Zist Fanavari Novin Biotechnology Institute, Isfahan, Iran

Introduction: Although fewer people have been diagnosed with Gastric Cancer (GC) in the last 50 years, it is still one of the most common cancers worldwide. The incidence of this cancer has declined due to a better diet and successful treatment of H.pylori infection. One of the principal challenges in GC treatment is early diagnosis to increase the survival rate. To be more specific, the pre-metastatic diagnosis survival rate is over twice the metastatic survival rate. Therefore, utilizing reliable biomarkers would highly improve the prognosis and treatment of this illness. Defining a competitive endogenous RNA (CeRNA) network provides valuable biomarkers and boosts the treatment process. CeRna theory claims that RNAs compete for a limited number of miRNAs; this competition affects the regulation of the cell. In cancer, the relationship between the components of this network changes (compared to the normal condition) and provides valuable information about the disease and its stage. This study has employed bioinformatics analysis using RStudio to target novel biomarkers for diagnosis and curing CG.

Methods: First, GSE79973 raw data was downloaded from Gene Expression Omnibus (GEO). Using RStudio, an in-depth analysis was performed to obtain differentially expressed genes. The most significant genes (|logFC| > 2 and adjusted p-value< 0.05) were selected and taken to miRWalk 2.0 to find target miRNAs. To find suitable lncRNAs, miRNAs were searched in LncBase v.3 and several lncRNAs were found. Additionally, to ensure that the lncRNAs are highly significant in Gastric Cancer, the lnCAR database was employed At last, Cystoscope software 3.8.2 was used to show the interaction between the components of the ceRNA network.

Results: After careful analysis of ten pairs of gastric cancer tissue and adjacent non-tumor mucosa (GSE79973), a total number of 788 differentially expressed genes (DEGs) were detected. DEGs with adjusted p-value < 0.05 and |logFC| > 2 were considered significant. 20 of the hub genes with the lowest adjusted p-value were taken to miRWalk 2.0. The miRwalk 2.0 database provided target miRNA for the chosen hub genes. Score and number of pairings were considered factors for a suitable miRNA. THY1(Thy-1 cell surface antigen) demonstrated a connection with hsa-miR-324-3p in

miRwalk. The picked miRNA was searched in LncBase v.3 and H19, GAS5, and DLEU2 were found. To make sure that the lncRNAs are significant in Gastric cancer, lnCAR was used to find the level of expression of lncRNAs. Then, using TANRIC database the connection of H19 and THY1 was also proved with the correlation of 0.4. In addition, the BioPlanet 2019 database confirmed that THY1 is a component of Integrin beta-2 pathway which is involved in tumor progression.

Conclusion: According to the previous analysis, there might be a CeRNA network between THY1, H19, and hsa-miR-324-3p. Moreover, the involvement of THY1 in a CeRNA network, as well as a signaling pathway, reinforces the possibility of THY1 being a reliable biomarker for diagnostic and prognostic goals.

Keywords: Microarray, Gastric cancer, THY1, Bioinformatics, CeRNA

Harnessing Microalgae as New Carriers in Cancer Therapy (Review)

Fatemeh Khavari,[1] Massoud Saidijam,[2] Mohammad Taheri,[3] Fatemeh Nouri,[4,*]

1. Student Research Committee, Hamadan University of Medical Sciences, Hamadan, Iran
2. Research Center for Molecular Medicine, Hamadan University of Medical Sciences, Hamadan, Iran
3. Department of Medical Microbiology, Faculty of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran
4. Department of Pharmaceutical Biotechnology, School of Pharmacy, Hamadan University of Medical Sciences, Hamadan, Iran

Introduction: Cancer is the cause of 171.2 of 100,000 deaths each year. However, a major challenge in cancer therapy is the impact of anticancer drugs on normal cells and tissues. Using drug delivery systems is considered to be an effective approach to the reduction of toxicity and improving the therapeutic efficacy of drugs, especially in cancer therapy. Using synthetic NPs for the delivery of anticancer drugs is an important approach to the improvement of chemotherapy effectiveness. However, these materials may be toxic and have some environmental disadvantages. Today, emphasis is placed on the use of marine resources in biomedicine. Microalgae are major sources of various polysaccharides, which could be converted into NPs and use hydrophilic groups on the surface to interact with biomolecules.

Methods: The bibliographic search was performed on PubMed, Scopus, and Web of Science databases. Any language or date restrictions were not applied. Identified studies were screened by title, abstract, and full text. During the reviewed articles in 2020, if we identified a new article, we would include it in our study.

Results: Diatom is a eukaryotic unicellular microalga with a unique cell wall known as a frustule. Frustule structure is composed of silica and could be easily protected, functionalized, and engineered for successive drug loading and delivery. Terracciano et al. used biofunctionalized diatom nanoparticles (DNPs) for drug loading and release studies of sorafenib, a poorly water-soluble anticancer drug. They found DNPs functionalized with ATPES(3-Aminopropyl) triethoxysilane and polyethylene glycol (PEG) showed excellent cellular uptake and better-sustained drug release profile. Diatomites activated by oxidizing acids have been used as a carrier of ophiobolin A (anticancer compound of fungal origin), extending the release of this agent. Furthermore, Diatomite NPs are effective in the transport of siRNA inside human epidermoid cancer cells (H1355) to silence gene expression. These

nanocarriers could also be loaded with one or more different molecules and improve the delivery of antitumor biomolecules and drugs.

Conclusion: Diatom shells have unique 3D structures and are used for the production of NPs for drug and biomolecule delivery. Different morphology and functionalization could enhance drug loading and release from DE NPs. Several studies have investigated modified diatomites for the specific delivery of drugs (DOX, camptothecin, paclitaxel) in the treatment of colon and breast cancer, proposing positive outcomes. Further investigation and clinical trials are still required in this regard.

Keywords: Microalgae, Drug delivery, Cancer

Has-miR-213-3p/NEAT1 axis of a ceRNA network promotes the development of pancreatic cancer by regulating Pi3k-Akt signaling pathway and TGF-beta signaling pathway: an integrated bioinformatics and systems biology analysis (Research Paper)

MohammadHossein Teymouri,[1] Mohammad Rezaei,[2] Mansoureh Azadeh,[3,*]

1. Zist Fanavari Novin Biotechnology Institute, Isfahan, Iran
2. Zist Fanavari Novin Biotechnology Institute, Isfahan, Iran
3. Zist Fanavari Novin Biotechnology Institute, Isfahan, Iran

Introduction: More than 90% of pancreatic cancer cases are pancreatic ductal adenocarcinoma (PDAC) with a 5-year survival rate of approximately only 5%. In recent decades, miRNAs and lncRNAs have been studied and are considered as impactful biomarkers in cancer. Therefore, in this bioinformatic approach, the goal was to spot and determine a biological network of genes, miRNAs and lncRNAs which have a notable influence on progression of PDAC.

Methods: To begin with, GSE15471 has been chosen from NCBI Gene Expression Omnibus (GEO) and was analyzed with R Studio in order to find genes with significant increase in expression regulation. INHBA, THBS2, NTM and SULF1 were selected and by using miRWalk database, plenty miRNAs were found for each of these genes. Furthermore, by using Venny 2.1 a mutual miRNA between these 4 genes was identified which was hsa-miR-214-3p. in addition, with the purpose of finding lncRNAs related to this network, the miRNA was searched in LncBase 3.0 and DLGAP1-AS1 and NEAT1 were selected as suitable lncRNAs. Ultimately, the pathways that these genes were involved in were analyzed and studied to find their role in Cancer. At last, Cystoscope software 3.8.2 was used to show the interaction between the components of the ceRNA network.

Results: Based on the analysis that were carried out, the mentioned 4 genes were selected and by using Kegg database their pathways were examined individually. INHBA is involved in Cytokine-cytokine receptor interaction, TGF-beta signaling pathway and Signaling pathways regulating pluripotency of stem cells. One of the most crucial pathways in which THBS2 has a role is PI3K-Akt signaling pathway which is consequential in development of cancer. With the shared miRNA with INHBA and THBS2 and lncRNAs that have interactions with it, NTM and SULF1 have increased expression levels as well and could have a role in cancer progression.

Conclusion: Contemplating the above paragraphs, it is concluded that INHBA, THBS2, NTM and SULF1 with has-miR-214-3p and its CeRNAs

(competing endogenous RNAs) DLGAP1-AS1 and NEAT1 act as a biological network with important role in cell energy and growth pathways. Thus, these findings could provide a promising therapy method for treatment of PDAC patients.

Keywords: ceRNA - Systems biology - Pancreatic ductal adenocarcinom - Bioinformatics

Health and nutrition (Review)

Amirhosein zand ,[1,*]

1. faculty of pharmaceutical science

Introduction: Low vitamin D status is a widespread problem in the US [1, 2]. Research has shown that serum vitamin D concentrations previously considered in the normal range are not sufficient for optimal health [3]. Vitamin D plays a role in a wide range of ailments such as osteoporosis, cancer, cardiovascular diseases, and diabetes [4, 5]. Recently, a role for vitamin D in cognitive function and mental health has been reported [6, 7]. Vitamin D concentrations have been shown to be low in patients suffering from mood disorders and have been associated with cognitive function [8, 9]. Depression is one of the leading causes of disability in the US among young adults. In the US, in a given year, about 26% of population, aged ≥18 years suffer from a diagnosable mental disorder and about 6% (1 in 17) suffer from a serious mental disorder [10]. Several mechanisms of action have been proposed to explain the association between vitamin D and depression. The role of calcitriol or 1, 25 dihydroxy cholecalciferol, the bioactive form of vitamin D, in brain tissue has been confirmed by the presence of vitamin D receptors (VDR) and hydroxylases in various brain regions [11, 12]. One area where VDR and hydroxylases have been found is the amygdala, which is the center of the limbic system, where behavior and emotions are regulated [13]. Vitamin D has been reported to exert a neuroprotective function through several mechanisms. Calcitriol regulates calcium concentrations intra- and extracellularly in neurons, consequently reducing toxicity caused by excess calcium [14–16]. A few studies have found an association between serum vitamin D concentrations and depression [17–20]. Light therapy has been shown to improve the depression in adjunction with antidepressants, which may be in part due to improved vitamin D synthesis associated with light therapy [21]. Majority of the studies relating vitamin D status with depression are based either on a small sample size or non-representative of the US population. Very little is reported on the association between vitamin D concentrations and depression in young adult US population. Overall, the previous studies on the association between vitamin D status and depression yielded equivocal results [22–25]. Therefore, the aim of this study was to investigate the association between serum vitamin D concentrations (25 hydroxy cholecalciferol) and depression in a large, nationally representative sample survey of the US population, the Third National Health and Nutrition Examination Survey (NHANES III).

Methods: Data from the third National Health and Nutrition Examination Survey were used to assess association between serum vitamin D and depression in 7970 non-institutionalized US residents, aged 15-39 y.

Assessment of depression was done using the Diagnostic Interview Schedule developed by the National Institute of Mental Health. After accounting for several confounding variables in multivariate logistic regression analysis, we estimated odds ratios (OR) for having depression in vitamin D deficient persons in comparison to vitamin D sufficient persons

Results: Women, non-Hispanic blacks, persons living below poverty, persons who did not consume supplements, persons living in South and West regions and in urban areas, persons with higher BMI, and persons with current depression had higher prevalence of vitamin D deficiency compared to their counterparts. OR for having current depressive episodes in persons with serum vitamin D ≤ 50 nmol/L is significantly higher relative to those with serum vitamin D ≥ 75 nmol/L (OR = 1.85; P = 0.021).

Conclusion: In this large population based study, likelihood of having depression in persons with vitamin D deficiency is significantly higher compared to those with vitamin D sufficiency. Early diagnosis and intervention are paramount because coexistence of vitamin D deficiency and depression has serious negative consequences on health.

Keywords: vitamin D , third

Healthcare practitioners' Knowledge of Lymphedema: A Systematic Review (Review)

Hossein Yarmohammadi,[1] Masood Soltanipur,[2] Amirhossein Rooddehghan,[3] Amirabbas Sarafraz,[4] Seyed Fatah Mahdavi Anari,[5,*]

1. Medical Students Research Committee, Shahed University, Tehran, Iran
2. Medical Students Research Committee, Shahed University, Tehran, Iran
3. Faculty of Paramedical Sciences, Islamic Azad University, Tehran, Iran
4. First Saint Petersburg Pavlov State Medical University, Saint Petersburg, Russian Federation
5. Department of Dermatology, Shiraz University of Medical Sciences, Shiraz, Iran

Introduction: Lymphedema is neglected in medical education and a review on HealthCare Practitioners' (HCPs) knowledge is necessary to shed light on gaps and to provide evidence for establishing educational programs on lymphedema.

Methods: This systematic review was performed based on the PRISMA guideline in Pubmed, Scopus, Web of Science, and Google Scholar databases. There was no limitation on the type of lymphedema or HCPs. The quality assessment was performed based on QATSDD. Data regarding studies characteristics, questionnaire context, and findings of the study were summarised from each article.

Results: After the screening, 12 articles were included that 9 were cross-sectional, 2 were qualitative studies and one was an interventional pilot study. Breast cancer and another cancer-related lymphedema, lymphatic filariasis, and podoconiosis were included and the majority of articles were focused on primary HCPs. The overall knowledge was low and average in 5 and 7 articles respectively and prior education was a significant factor related to higher knowledge of lymphedema.

Conclusion: Structured education of lymphedema is needed to increase the knowledge of HCPs and to enhance their collaboration in multidisciplinary care teams. Improvement of HCPs' knowledge may lead to better outcomes of lymphedema patients' management which are neglected.

Keywords: Lymphedema, Knowledge, HealthCare Practitioner, Education

Helicobacter pylori cagL Polymorphism D58E59 in gastric cancer, peptic ulcer and gastritis in north of iran (Research Paper)

Mina Rezaee Cherati,[1,*] Hamid Reza Nouri ,[2] Seyed Jalal Zargar,[3]

1. Department of Cell & Molecular Biology, Kish International Campus, University of Tehran, Kish Island, Iran
2. Immunoregulation Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran
3. Department of Cell & Molecular Biology, School of Biology, College of Science, University of Tehran, Tehran, Iran

Introduction: Gastric cancer and peptic ulcer are the most important gastrointestinal disorders in the world, including Iran, that H. pylori is an important risk factor in the development of these diseases. The cagL encoded by cagL genes and expressed in pathogenicity island (cagPAI) that this protein plays a fundamental role in binding to host cells. Hence, the aim of this study was to determine cagL gene polymorphisms in patients with H. pylori-positive and its relationship with peptic ulcer and gastric cancer in north of Iran.

Methods: This cross-sectional study was conducted on 100 patients with gastric cancer, peptic ulcer and gastritis, which was referred to the Shahid Beheshti and Ayatollah Rouhani hospitals of Babol in 2015.During endoscopy, gastric biopsies were taken and samples were saved in sterile conditions. DNA was extracted from the tissue samples and detection of H. pylori in biopsy samples were confirmed using PCR with glmM primers. The cagL gene was amplified by gene-specific primers and, then was confirmed by electrophoresis its. After that, DNA was extracted from agarose gel and DNA sequencing was done

Results: In the present study, 78.26% (18/23) of patients with gastric cancer, 46.6% (14/30) from gastritis and 74.4% (35/47) of peptic ulcer patients were positive for H. pylori which demonstrates the H. pylori infection in gastric cancer and peptic ulcer were significantly higher than gastritis ($P<0.05$). In total, 67 sample were investigated for presence of cagL. The gene positivity of the cagL was 71.6% (48/67) in patients were infected with H. pylori. Frequency of cagL in patients with gastric cancer and peptic ulcer compared to patients with gastritis was not significant ($p>0.05$). Study of cagL polymorphisms showed that people with peptic ulcers compared to patients with gastric cancer or gastritis patients had significantly amino acid aspartic acid (D) at position 58, while the amino acid asparagine (N) in patients with gastric cancer has been in this position. Polymorphism at position 60 also showed that people with peptic ulcer compared to other subjects significantly had the amino acid isoleucine (I) in this position. The presence of the amino

acid glutamine (Q) and asparagine (N) at position 62 and 122 respectively increased (P <0.05) risk of gastric cancer and peptic ulcer development. Also, the amino acid valine (V) was significantly placed in 134 position in patients with gastric cancer compared to peptic ulcer or gastritis.

Conclusion: Infection with cagL positive H. pylori increases risk of serious gastro duodenal diseases such as peptic ulcers and gastric cancer. Also, presence of the amino acids: aspartic acid, isoleucine, glutamine and asparagine at position 58, 60, 62 and 122, respectively increase the risk of peptic ulcer development in H. pylori infected patients. However, presence of the amino acid asparagine, methionine, glutamine and asparagine at the same position alongside valine in position of 134 increase the risk of gastric cancer development

Keywords: Peptic ulcer, Gastric cancer, Gene cagL, Polymorphism

Hemophilia, care and prevention of the birth of a sick child (Review)

Mahya Badbarouni,[1,*]

1. Azad university of Dezful

Introduction: Hemophilia is an inherited disease of chromosome X. It is 80% related to factor eight diseases (hemophilia A) and 20% related to factor 9 (hemophilia B). These include: risk of bleeding from the joints (feet, knees, elbows), hematoma or soft tissue bruising, postoperative bleeding, tendency of the body to bleed from the nose and mouth due to minor injuries, blood in the urine and feces, and bleeding Cerebral hemophilia A and B are inherited diseases that are passed on from the X chromosome gene. Women have two X chromosomes and men have one X chromosome and one Y chromosome. A woman carrying a hemophilia gene that she has on one of her X chromosomes is 50% more likely to pass the defective gene to her children. Men who have a defective gene (with hemophilia) do not pass it on to their sons but to girls. It can be passed on through the father. Women who inherit the gene pass it on to their children 50% of the time, with the interpretation that these women do not have an active hemophilia gene, meaning they do not have an active hemophilia problem, but have frequent bleeding. Severe bleeding after surgery and dentistry and severe menstrual bleeding occur in these people. About 1.3% of hemophilia patients have no family history of the disease. These cases are the result of spontaneous gene defect in women. Care for hemophilia patients: In general, prevention of bleeding and in case of bleeding, its treatment within the first two hours and treatment of bleeding that is mild can only be done at home, otherwise refer to special centers should be done. Improve lifestyle. Intramuscular injections and non-steroidal anti-inflammatory drugs should be avoided. Regular exercise in hemophilia patients and muscle strengthening is very effective in the process of recovery and protection. Patients' treatment also depends on the level of coagulation factors. The person can be different. For example: the method of replacing coagulation factors, stimulating the body to produce coagulation factors (desmopressin), clot-retaining drugs, surgery in need, ie damage to the joints, vaccination, etc.

Methods: BYE REVIEW AND STUDT OTHER ARTICLES

Results: There is generally no definitive cure for hemophilia patients, but by following the simple tips, patients can avoid bleeding and serious injuries to experience a healthier life.

Conclusion: the best time to perform hemophilia genetic tests and determine a person's genetic status is before pregnancy, because in some cases

determining a person's genetic status is complex and takes time. So before trying to conceive, couples should go to the lab. If the condition is known. It is possible to diagnose more quickly in pregnancy.

Keywords: Hemophilia, care, X chromosome disease, defective gene

Histological survey on topical effect of Skin Pistachio hydroethanolic extract ointment on excisional wound healing in rat (Research Paper)

Leila Zarei,[1] Masoumeh Pourjabali,[2] Asghar Rajabzadeh,[3,*]

1. Associate Professor,Department of Anatomical Sciences, Faculty of Medicine, Lorestan University ofMedical Sciences, Khorramabad, Iran.
2. Assistant Professor,Department of Pathology, Faculty of Medicine, Urmia University of MedicalSciences, Urmia, Iran.
3. Assistant Professor,Department of Anatomical Sciences, Faculty of Medicine, Lorestan University ofMedical Sciences, Khorramabad. Iran.

Introduction: Wound healing is one of the most important issues that mankind faces from the beginning of creation. Therefore, trying to find compounds that affect the wound healing has the least side effects is one of the human aspirations and in this regard, medicinal plants are of particular importance. In this study, the effect of Skin pistachio hydroalcoholic extract ointment on the healing process was carried out based on planetary and histological studies in a 14-day period after the wound.

Methods: In order to evaluate the planter size, 20 healthy rats were randomly assigned into 5 groups of 4, including control group (open wound without any intervention and treatment), control group (open wound with ointment without extracts), treatment group 1 with concentration 1 % of ointment containing pistachio extract, the second group with 2% concentration of ointment containing skin pistachio extract and the treatment group 3 with 4% concentration of ointment containing pistachio extract were divided. The wounds are washed with normal saline solution for 10 days (daily) and will be applied to ointment groups.

Results: The results showed that wound treatment with this ointment in the experimental group resulted in a significant increase ($p < 0.05$) in the percentage of wound healing. Also, there was a significant difference in the thickness of skin and collagen diameter and reduction of edema ($P < 0.05$) was observed. Comparison of the results of neutrophil count, fibroblast, and macrophage was observed on day 14 in the treated groups with skin pistachio extract and control ($p < 0.05$). These results were indicative of accelerated wound healing in treated specimens.

Conclusion: According to the results of this study, an ointment containing skin pistachio extract can have healing effects on the wound created in the skin of the rat.

Keywords: Full thickness wound, Wound healing, hydroalcoholic extract, skin Pistachio, Histology, planimetric

Histometrical evaluation of lead acetate effects on kidney and testes of male diabetic rats due to cinnamon extract administration (Research Paper)

Fattahian Rahmatollah,[1] Forouhar Majd Kianoush,[2] Badkoubi Amirhossein,[3,*] Changaniyan Khorasgani Zahra,[4]

1. Associate Professor, Department of Basic Sciences, Faculty of Veterinary Medicine, Shahrekord University, Shahrekord, Iran
2. Student of Veterinary Medicine, Faculty of Veterinary Medicine, Shahrekord University, Shahrekord, Iran
3. Student of Veterinary Medicine, Faculty of Veterinary Medicine, Shahrekord University, Shahrekord, Iran
4. Student of Veterinary Medicine, Faculty of Veterinary Medicine, Shahrekord University, Shahrekord, Iran

Introduction: Chronic hyperglycemia that is known as a hallmark of diabetes, have involved a majority of peoples around the world. The cytotoxic effect of Lead acetate that is released in water and the environment of Developed and under-developing countries, has been proved. Cinnamon contains natural antioxidant extracts. It has been known for it's major component, Cinnamaldehyde. Therefore, we investigate on Histometrical effects of lead acetate on testes and kidneys of male rats treated with cinnamon extract.

Methods: 48 male rats that have been weighted in a range between 200±20gm, were used in this investigation. All animals' examination were carried out under the protocols that approved by the veterinary faculty of Shahrekord university. At the end of this examination, the kidneys and testes of rats were collected and processed. All specimens were stained by H&E staining. After the data collection, they have been analyzed by the latest version of SPSS with consideration of $P<0.05$ significance.

Results: Histometrical analysis of cinnamon extract administrated groups, indicates significant tissue changes. Also, this investigation approves predominant Histometrical changes in examined tissues due to oral administration of lead acetate.

Conclusion: The potential role of cinnamon in management of the hyperglycemia has been indicated in many in vitro studies on both human and animal cases. Cinnamon treats diabetes by activating insulin-receptor-kinase and inhibiting insulin-receptor-phosphatase, resulting in a maximal response of insulin-receptor-phosphatase and subsequently increase insulin sensitivity. The enzyme; insulin-receptor-kinase; facilitates insulin binding to cells and another enzyme, insulin-receptor-phosphatase, can cease this process.

Keywords: Cinnamon, Histometrical Investigation, Lead acetate, Kidney, Testes

Histopathological changes of different doses of Nickel chloride on Wistar rat's liver (Research Paper)

Ghazaleh sadeghnezhad,[1] Seyed Mohammad Hosseini,[2,*] Sohrab kazemi,[3]

1. Department of Pathology, Islamic Azad University, Babol Branch, Babol, Iran
2. Department of Pathology, Islamic Azad University, Babol Branch, Babol, Iran
3. Cellular and Molecular biology research center, health research institute, Babol University of Medical Sciences, Babol, Iran

Introduction: The nickel compounds are important in modern industry. Due to the use of nickel and nickel chloride in medicine, preparation of medical composites in pharmacy, factories and waste incineration, pharmaceutical industry, food, hydrogenation of vegetable oils, everyday environmental contact or job contact can lead to long-term risks and cell damage, or cancer. Exposure to nickel chloride (NiCl2) can cause hepatotoxicity.

Methods: Adult female albino rats of Wistar strain (200–220 g) were used for the experiment. Thirty-two female Wistar rats were divided into four groups evenly. The duration of the test was 20 days. The Control group received nothing but water intraperitoneally. Nickel was given to three other groups by IP 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 anesthetized by ketamine (30 mg/kg body weight, intramuscularly) and rats were euthanized under general anesthesia by Ketamine and Xylazine. Then, liver specimens were obtained for hematoxylin and eosin staining and evaluated microscopically.

Results: The Control group indicated normal livers, Nickel treated groups have shown numerous pathologic lesions including infiltration of inflammatory cells, hyperemia, and vacuolar degeneration, whose intensity gets much severer by increasing the dose of Nickel and also, the dose of 25mg/kg illustrated the worst pathological condition amongst all groups.

Conclusion: According to results clearly demonstrate that the adverse effects of Nickel are dose-related.

Keywords: Nickel, Histopathology, liver, Wistar rat

HIV associated neurocognitive disorder (HAND): A systematic review study (Review)

Pedram Bolbolizade,[1] Fatemeh Zahra Seyedkolbadi,[2,*] Fatemeh Zamani,[3] Faezeh Mirshahi,[4] ali salimi asl,[5]

1. Student Research Committee, Faculty of Para Medicine, Hormozgan University of Medical Sciences, Bandar Abass, Iran
2. Student Research Committee, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
3. Student Research Committee, Faculty of Para Medicine, Hormozgan University of Medical Sciences, Bandar Abass, Iran
4. Student Research Committee, Faculty of Para Medicine, Hormozgan University of Medical Sciences, Bandar Abass, Iran
5. Student Research Committee, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

Introduction: According to the World Health Organization (WHO), the number of people infected with the human immunodeficiency virus (HIV) in 2019 was about 38 million people. These days, due to the use of combination antiretroviral therapy (cART), life expectancy has increased in these people and HIV has changed from a deadly disease to chronic disease. HAND includes asymptomatic neurological disorder (ANI), Motor neurological disorder (MND), and HIV-associated dementia. But, these days, due to the use of combined antiretroviral therapy (cART), the prevalence of severe manifestations has decreased, but mild manifestations are still common in the affected community. In this study, we intend to conduct a comprehensive and systematic review of existing studies in various fields of these disorders, including; Risk factors, their diagnostic methods, the epidemiology of disorders, and finally the treatment of HIV-associated neurological disorders.

Methods: In this study, our search was based on English and was conducted from 2015 to 2021 and was searched in PubMed, Science Direct, and Scopus databases. The keyword used for the search included HIV-associated neurocognitive disorder, HAND, cART. In the initial search, we came across 2,500 articles, and after reading the titles and summaries, we reduced it to 100. Finally, for the final data, we reduced the full text to 21 articles after reading it.

Results: We categorized the results of our study into sub-categories, which include; Risk factors are pathogenicity, clinical manifestations, diagnosis, and epidemiology We examined these subheadings from different angles in the obtained articles, which we tried to cover completely, even with some limitations, to compare different examples of them and consider a good solution and diagnosis for it. In Risk factor, show some of the things that could

increase the chance of developing these diseases and the clinical manifestations shows the most common characteristics of the patient who had developed HAND and In Diagnostics, we try to give you the common prosses that a doctor goes through to Diagnoses these diseases. Also, In the pathogen section, we examined the progression of the disease in patients and in the epidemiology section, we comprehensively examined its prevalence in Iran and abroad.

Conclusion: Although significant progress has been made in the HAND reviewed subheadings, many questions remain about the disease, and many of the methods that have been introduced and used in the diagnosis are not 100% certain and also can not yet fully withstand this epidemic. Let the disease stand and we hope to find more progress and more definitive solutions to it in the coming decades and apply it.

Keywords: HIV associated neurocognitive disorder, HAND, cART

HNF1A: an important transcription factor in gastric cancer (Research Paper)

Sadra Salehi-Mazandarani ,[1] Mohammad Hossein Donyavi,[2] Parvaneh Nikpour,[3,*]

1. Department of Genetics and Molecular Biology, Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
2. Department of Cell and Molecular Biology and Microbiology, Faculty of Biological Science and Technology, University of Isfahan, Isfahan, Iran
3. Department of Genetics and Molecular Biology, Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

Introduction: Gastric cancer (GC) is one of the most common cause of cancer-related death in the world. Although many studies have dealt with the molecular and cellular mechanisms of GC, it has not been completely understood. Investigation of regulatory molecules such as transcription factors can give us a deeper view of molecular alterations happening in GC. It also can help us to identify new biomarkers and therapeutic targets for this type of cancer. In this study, we performed bioinformatic analyses to reveal important transcription factors as well as signaling pathways and gene ontologies in GC.

Methods: RNAseq data of GC were retrieved from The Cancer Genome Atlas (TCGA) database using TCGAbiolinks package in the RStudio software. Spearman correlation (correlation > 0.6) among the samples was evaluated by TCGAanalyze_Preprocessing function of TCGAbiolinks package. Then data were normalized and not-correlated RNAs were filtered by TCGAanalyze_Normalization and TCGAanalyze_Filtering functions of TCGAbiolinks package, respectively. TCGAanalyze_DEA was utilized to identify differentially expressed RNAs (DERs) according to adjusted p-value < 0.01 and logFC > 2. DERs were annotated by biomaRt package and differentially expressed mRNAs (DEMs) were identified. Transcription factors regulating the DEMs were then predicted by the FunRich software (version 3.1.3). Furthermore, enrichment analyses on the DEMs were performed using Enrichr online database.

Results: RNAseq data from 407 GC samples including 32 paracancerous and 375 cancerous samples were retrieved from the TCGA database. All samples showed high correlation with each other. According to adjusted p-value < 0.01 and logFC > 2, 1836 differentially expressed RNAs between cancerous and paracancerous GC samples were identified. DERs were annotated and 1546 differentially expressed mRNAs including 734 up- and 812 down-regulated mRNAs were extracted. Five predictive transcription factors regulating the DEMs were identified which among them only Hepatocyte Nuclear Factor 1-Alpha (HNF1A) was significantly (p-value <

0.05) correlated with DEMs by regulating 8.2 % of them. Significant KEGG pathways and GO terms relating to the DEMs were then identified. Neuroactive ligand-receptor interaction, fat digestion and absorption, protein digestion and absorption, metabolism of xenobiotics by cytochrome P450 and bile secretion were the most significant KEGG pathways. Besides, epidermis development (GO:0008544), receptor ligand activity (GO:0048018) and cornified envelope (GO:0001533) were the most significant GO terms relating to biological process, molecular function and cellular component, respectively.

Conclusion: In the current study, we identified HNF1A as an important transcription factor in GC which regulates a lot of critical genes. Although various studies have revealed important roles of HNF1A in different cancers, few studies have dealt with its functions in GC. It has been reported that HNF1A induces the expression of HLA Complex Group 18 (HCG18) gene. Then, overexpression of HCG18 by preventing the binding of miR-152-3p to DNAJB12 leads to upregulation of DNAJB12 by which promotes GC. Furthermore, we revealed significant signaling pathways and gene ontologies correlating with GC. Future studies are needed to increase our insight into the cellular and molecular aspects of GC which are modulated by transcription factors.

Keywords: Gastric cancer, Transcription factor, mRNA

How can COVID-19 affect the nervous system?: A comprehensive review study (Review)

Mina AkbariRad,[1,*]

1. Assistant Professor of Internal Medicine, Department of Internal Medicine, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

Introduction: Today the novel coronavirus disease (COVID-19) becomes a great disaster all over the world. According to the current knowledge, this virus can cause some molecular processes which lead to neuroinflammation, neurodegeneration, and neuronal injury. In this study, we briefly reviewed these possible molecular processes and the clinical neurological manifestations of the COVID-19.

Methods: A comprehensive search was done through electronic databases including PubMed, Embase, Scopus, and Web of Sciences with the related MeSh terms. Original and review studies, which studied on adults, were included, also the references of the review studies were rechecked to reduces the risk of bias and missing any related article. Due to the possible effects of interventions, randomized clinical trial studies were excluded from the final review.

Results: According to the cytokine storm and immune responses caused by COVID-19, different injuries and damages are predictable. An increase in IL-6, TNF-α, and activation of mast cells can lead to inflammation, especially neuroinflammatory processes. The clinical manifestations of these processes are evaluated by several studies that determined more frequent neurologic disorders in moderate and severe infected patients. Although confusion was observed too frequently in COVID-19 patients, other neurological manifestations such as dizziness, anosmia, visional problems, ataxia, and cerebrovascular diseases were observed in some cases persistently. It is important to note that there have not been found any significant differences between infected patients and non-infected ones in terms of their brain MRIs.

Conclusion: Based on the novelty of the current infectious disease, there is little knowledge about its mechanisms and clinical manifestations, especially about the nervous system. However, more studies are needed to clarify the exact effects of the COVID-19 on the nervous system, but it is certain that this virus potentially has destructive effects on our nervous system.

Keywords: COVID-19, Neuroinflammation, Neurodegeneration, Neurological manifestations

Human embryonic stem cells: applications in regenerative medicine (Review)

Faezeh Tolouei,[1,*] Danial Safarpoor,[2]

1. Department of Genetics, Faculty of Basic and Medical Sciences, Islamic Azad University, Science and Research Branch, Zanjan, Iran
2. Faculty of Veterinary Medicine, Islamic Azad University, Karaj Branch, Karaj, Iran

Introduction: Human embryonic stem cells (hESCs) were successfully generated in 1998 by culturing inner cell mass cells isolated from human blastocyst. hESCs have various clinical applications. These cells can be differentiated into a variety of desirable replacement tissues for the treatment of several diseases by transplantation therapy. hESCs also serve as appropriate models for studying early human development, infant cancers and congenital anomalies. Since the hESCs are pluripotent cells, human embryogenesis and the effects of potential teratogens can be studied. hESCs are also used for screening and testing potential drugs for the pharmaceutical industry. The directed derivatives of hESCs, such as cardiomyocytes have become attractive platform to evaluate cardiotoxicity.

Methods: This study has benefited from digital libraries resources published from 2005 to present.

Results: hESCs are described as pluripotent cells because they are able to differentiate into all three germ layers of the embryo and their derivatives; for example, pluripotent hESCs can be differentiated into neuronal cells, cardiac cells, liver cells, adrenal cells, keratinocytes, insulin-producing cells, and islet-like organoid. The transplantation of hESCs and their differentiated cells was tested in the animal models of Parkinson's disease, cardiovascular disease, stroke, diabetes, and spinal cord injury. Several clinical studies have evaluated the therapeutic effects of hESCs; for example in patients who were suffering from spinal injury, macular degeneration disease or type 1 diabetes. Although hESCs have great potential for the treatment of various degenerative diseases, the application of them has faced several challenges such as teratoma formation, immunorejection, and ethical, social, and political aspects.

Conclusion: hESCs have great potentials for use in regenerative medicine, although many obstacles still have to be overcome.

Keywords: human embryonic stem cells, pluripotent cells, differentiation, transplantation, disease.

Human menstrual blood stem cells-derived exosomes inhibit endometriosis through apoptosis induction (Research Paper)

Seyedeh Saeideh Sahraei,[1] Faezeh Davoodi asl,[2] Naser Kalhor,[3] Hoda Fazaeli,[4] Mohsen Sheykhhasan,[5] Azar Sheikholeslami,[6,*]

1. 1. Department of Reproductive Biology, the Academic Centre for Education, Culture and Research, Qom Branch, Qom, Iran
2. 2. Department of Mesenchymal Stem Cells, the Academic Centre for Education, Culture and Research, Qom Branch, Qom, Iran
3. 2. Department of Mesenchymal Stem Cells, the Academic Centre for Education, Culture and Research, Qom Branch, Qom, Iran
4. 2. Department of Mesenchymal Stem Cells, the Academic Centre for Education, Culture and Research, Qom Branch, Qom, Iran
5. 2. Department of Mesenchymal Stem Cells, the Academic Centre for Education, Culture and Research, Qom Branch, Qom, Iran
6. 2. Department of Mesenchymal Stem Cells, the Academic Centre for Education, Culture and Research, Qom Branch, Qom, Iran

Introduction: Evidence suggests that retrograde menstrual blood which contains mesenchymal stem cells with differential gene expression compared to healthy women may play a role in endometriosis creation. Apoptosis suppression is one of the most important pathological processes of endometriosis. Also, exosomes have been found to play physiological roles as mediators of intercellular cell signaling between neighboring cells and even amongst distant tissues, and they may act independently but synergistically with soluble growth factors and hormones. The aim of the present study was to evaluate the effect of menstrual blood stem cells-derived exosomes (MenSCs-Exo) on apoptosis of endometriosis cells.

Methods: After confirm exosome extracted from healthy women's MenSCs (NE-MenSCs) culture supernatant, endometriosis cell (E-MenSCs) were treated with MenSCs-Exo. Apoptosis was analyzed by flowcytometry assay with annexin V-PI kit before and after treatment compared with NE-MenSCs, and the expression level of apoptosis genes (BAX and BCL2) were evaluated by real-time PCR.

Results: MenSCs-Exo surface markers (CD63 and CD81) were verified by flow cytometry and their size by DLS. MenSCs-Exo induced apoptosis in E-MenSCs by increasing annexinb V and propidium iodide (PI) ($P < 0.01$). Also, induction of apoptosis can be due to regulation of apoptosis related genes expression, including BAX ($P<0.05$) and BCL-2 ($P<0.01$). Moreover, the BAX/BCL-2 ratio was significantly higher ($R=1.995$; $p=0.04$) in treated E-MenSCs with MenSCs-Exo compared to E-MenSCs.

Conclusion: The results of the present study suggest that MenSCs-Ex can inhibit endometriosis progression at a mild-to-moderate level through induction of apoptosis. However, further studies on endometriosis cell signaling are necessary to achieve more accurate results.

Keywords: Endometriosis, Endometrial mesenchymal stem cells, Apoptosis, Exosomes

Human Papillomaviruses: Protein Oxidation Status (Review)

Shadi Setayeshi,[1,*]

1. Department of Medical Biotechnology, Faculty of Medicine, Babol University of Medical Sciences

Introduction: Human papillomaviruses (HPVs) are minute viruses that carry deoxyribonucleic acid (DNA) and are part of the Papillomaviridae family. More than 200 types of HPV have been established and classified into 29 genera, and most of them impact humans. HPVs linked with cancers of the uterine cervix, anogenital tumors, and head and neck malignancies. Oxidative stress (OS) represents an interesting and under-explored candidate as a promoting factor in HPV-initiated carcinogenesis. Worldwide, cervical cancer is the second most common malignancy in women, impacting about 35 of every 100,000 women. Attention given to the link between HPV and cancer was significantly raised when HPV types 16 and 18 were detected in cervical cancers and preneoplastic dysplasia, the lesions that can make a woman susceptible to malignancy of the uterine cervix. The aim of this study was to review available evidence evaluating the role of oxidative stress in Human papillomaviruses pathogenesis and cervical cancer.

Methods: An electronic search with time (recent ten years, up to 2021) and language (English) restrictions was conducted using PubMed in order to find relevant studies to the research question. The search terms included “Human Papillomavirus”, “HR-HPV”, “Reactive oxygen species (ROS)”, “Oxidative marker”, “Oxidative stress (OS)”, “cervical cancer “, were used individually or/and in various combinations to retrieve the relevant kinds of literature. Most recent studies including case-control studies, original research, and review articles were selected.

Results: For investigation of the oxidative stress role in the pathogenesis of diseases, mainly, studies have examined oxidative stress biomarkers in cervical tissue and modulation of proteins involved in the redox status regulation. In vivo study by redox proteomic approach showed five proteins which have been found to have increased levels of carbonyls in dysplastic samples (HPV-16 positive tissues) namely: cytokeratin 6, actin, cornulin, retinal dehydrogenase and GAPDH. One recent study looked at the role of the early expressed viral proteins E1, E2, E6, and E7 from HPV types 16 and 18 in the modulation of the redox state reported that the combined expression of E1 and E2 proteins increased ROS levels with the subsequent increase in the marker for DNA damage.

Conclusion: The upregulation of stress protein markers indicated that an increased oxidative environment occurs both in dysplastic and neoplastic tissues. However, in dysplastic tissues this condition resulted in oxidative modification of DNA and of proteins involved in cell morphogenesis and terminal differentiation such as CK6, actin, cornulin, RDH and GAPDH, providing the conditions for the neoplastic progression. Further studies are needed to better understand the effects of protein oxidation on cell transformation and cancer promotion.

Keywords: Human papillomaviruses, Oxidative stress, Reactive oxygen and nitrogen species, Antioxidant.

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

Identification of Antibacterial and Antifungal features of Tabrizicola aquatica gen nov., sp isolated from Qurugol Lake in mountain region of Azerbaijan. (Research Paper)

tahereh ebrahimi,[1] vahideh tarhriz,[2,*] azita dilmaghani,[3]

1. Department of Nano-Biotechnology, Pasteur Institute of Iran, Tehran, Iran
2. Molecular Medicine Research Center, Biomedicine Institute, Tabriz University of Medical Sciences, Tabriz, Iran
3. Department of Pharmaceutical Biotechnology, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran.

Introduction: Recently, resistant pathogenic microorganisms have become increasingly wide spread. The search for novel natural antibiotics is a viable solution to this problem. For this aim we investigated the antimicrobial ability of Tabrizicola aquatica, the novel bacterium isolated from Qurugol Lake located nearby Tabriz city, Iran.

Methods: The antimicrobial properties of Tabrizacola aquatica was investigated using well diffusion test. Tabtizicola aquatica was incubated at 40℃ in shaking incubator at 150 rpm for 14 days. The culture was centrifuged to obtain cell free supernatant, which was sterilized using 0.2 µm filter paper and lyophilized. Microorganisms were lawn and then wells were prepared over the agar plates. About 100 ml of the diluted lyophilized supernatant was added to the wells. The plates then were incubated at 37℃. After 48 hours, antimicrobial activity was defined by measuring the inhibition zone diameter.

Results: The bacterial filtrates had considerable antagonistic effect against Escherichia coli, Rhizobium radiobacter, Pseudomonas syringae, Erwinia amylovora, Botrytis cinerea, Neurospora crassa and Fusarium oxysporum. However, the filtrates did not show any inhibitory action on the Aspergillus flavus and Klebsiella pneumonia. The supernatant decreased the growth zone on Streptococcus aureus, Pseudomonas aeruginosa, Shigella flexneri, Xanthomonas camoestris and Bassilus cereos. The result of MIC against pathogens was found for Neurospora crassa in the 50 µg/mL.

Conclusion: The results, suggested that Tabrizicola aquatica and similar bacteria can be helpful to control freshwater natural water sources from pathogenic microorganism. Moreover, microbial natural products are still the most promising source of new antibiotics. Our results point out a scope for characterization of the metabolites and could be a candidate in the identification of novel antibiotics.

Keywords: Tabrizicola aquatica, Freshwater bacterium, Antibacterial and Antifungal Activity

Identification of bidirectional promoters as the major source of gene expression regulation-associated non-coding RNAs in breast cancer: in silico (Research Paper)

Mahboobeh Ramezani,[1,*] Fatemeh Shamsabadi,[2]

1. Department of Medical Genetics, School of Advanced Technologies in Medicine, Golestan University of Medical Sciences, Gorgan, Iran.
2. Department of Medical Biotechnology, School of Advanced Technologies in Medicine, Golestan University of Medical Sciences, Gorgan, Iran

Introduction: Identification of new potential biomarkers for early diagnosis and targeted therapy of breast cancer is demanded. In silico approaches improves our knowledge regarding to the cancer-associated genes. We focused, in this survey, on the bidirectional promoter genes in breast cancer.

Methods: RNA-Seq data for solid tumor and primary of breast tissues and the adjacent normal tissues were retrieved from the Cancer Genome Database. The expressed genes more than 2 fold obtained by DESeq package in R software. To recognize the transcription factors the GeneCards resource was used.

Results: Three bidirectional genes were identified; of which the WT1 (4.793) and TYMS (2.02) were greatly transcribed while transcription of RNPC3 (-0.79) decreased with P adjusted value of <0.001. Interestingly, the same transcription level of coding genes was observed for WT1-As (4.79) and TYMSOS (2.2) antisense, as well as AC095032.1 lncRNA (-2.57). These protein coding genes locate on the chromosomes 11, 18, and 1. Thirty similar transcription factors (TFs) were identified in these bidirectional promoters by the GeneCards resource (P<0.001). Only E2F1 was up-regulated more than 2 fold. However, among the significantly changed TFs, HDAC1, RNF2, and HDAC2 were introduced as hub genes by Cytoscape. These TFs were involved in DNA damage, metabolism of proteins, p53, and Notch signaling pathways.

Conclusion: Bidirectional non-coding RNAs (ncRNAs) generally regulate the expression of their protein-coding counterparts through epigenetic modification and promoter targeting. It can therefore be assumed that these bidirectional non-coding genes with different expression may serve an important roles in breast cancer. This finding has also important implications for developing tumor-specific targeting in cancer gene therapy

Keywords: Bidirectional promoter; breast cancer; WT1; TYMS; RNPC3.

Identification of gene expression profile of the Respiratory Syncytial Virus infection in children: A Network-based attitude (Research Paper)

Forough Tavakoli,[1,*] Talat Mokhtari-Azad,[2] Morteza Hadizade,[3] Vahid Salimi,[4]

1. Virology Department, School of Public Health, Tehran University of Medical Sciences, Iran
2. Virology Department, School of Public Health, Tehran University of Medical Sciences, Iran
3. Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
4. Virology Department, School of Public Health, Tehran University of Medical Sciences, Iran

Introduction: Respiratory Syncytial Virus is a common reason of acute lower respiratory infection in young children. The transition of clinical course from mild to severe infection is unpredictable. To gain insight into the immune pathways of the pathogenesis, we analyzed microarray transcription profiles of Respiratory Syncytial Virus infection.

Methods: We investigated tree microarray profile datasets (GSE117827, GSE41374 and GSE97743) to analyze the potential differentially expressed genes (DEGs) in nasal epithelium of children under two years old with Respiratory Syncytial Virus infection in two RSV positive-RSV discharge and RSV positive- healthy groups. KEGG pathways and Gene Ontology Enrichment and Functional Analysis was conducted using Enrichr and DAVID bioinformatics tool and GSEA software. Co-expression network and hub genes was identified by hmsic R package, MCODE and CytoHuba plugin of Cytoscape. Protein-protein interaction (PPI) network of DEGs was constructed by STRING and visualized by Cytoscape software.

Results: A total of 145 DEGs was identified in RSV- healthy group, including 93 upregulated and 52 downregulated genes. A total of 125 DEGs was identified in RSV- RSV discharge group, including 104 upregulated and 21downregulated genes. Gene functional enrichment analysis of DEGs from both RSV- healthy and RSV- RSV discharge indicated that upregulated genes were enriched in the immune responses and downregulated genes were enriched in the pathways related to metabolism including Valine_Leucine_AND_Isoleucine_Degradation, Butanoate and Pyruvate Metabolism and pathways related to cilium assembly, cilium organization and cilium movement.

Conclusion: The integrated bioinformatic analysis revealed RSV infection strongly induces innate and adaptive immune responses and decreases the

Ciliary function of respiratory tract. The hub differentially expressed genes may be potential biomarkers for RSV infection in children under two years old. Moreover, it can improve our insight into pathogenesis mechanisms and disease intervention of RSV infection.

Keywords: Respiratory Syncytial Virus , gene expression profile, pathway, microarray,transcription

Identification of immunodominant and conserved epitopes of heat shock protein 70 for cancer vaccine development (Research Paper)

Matin Kayyal,[1] Azam Bolhassani,[2,*]

1. Department of Biology, Science and Research Branch, Islamic Azad University, Tehran, Iran
2. Department of Hepatitis and AIDS, Pasteur Institute of Iran, Tehran, Iran

Introduction: Heat shock proteins are carriers of tumor antigens that trigger innate immunity, which in turn activates the adaptive immune system. Therefore, these proteins can be used as adjuvants to stimulate the immune system and develop immunotherapy approaches in the treatment of cancer. Heat shock protein-70 (HSP70), as a powerful immunostimulatory agent, may function as a sort of link between innate and adaptive immune response and stimulate cellular immunity.

Methods: In this study, the immunodominant and conserved epitopes of heat shock protein 70 (Hsp70) as an immunostimulatory agent were analyzed using different bioinformatics and computational tools. For this purpose, the cytotoxic T-lymphocyte (CTL) and helper T-lymphocyte (HTL) epitopes were predicted by NetMHCpan 4.0, NetMHCIIpan and IEDB. Then, the epitopes with the highest binding affinity scores were selected. After that, population coverage was estimated by IEDB tools for each epitope. Next, toxicity and allergenicity were measured by ToxinPred and AlgPred web servers, respectively. Moreover, secretion of cytokines as an important step was evaluated by web servers which established by Raghava's groups. Finally, for peptide-protein flexible Docking, GalaxyPepDock server was used to predict docking scores between MHC alleles and peptides.

Results: The CTL epitopes of HSP70 (113-FYPEEISSMVLTKM-126 and 285-SLFEGIDFYTSITR-298), and HTL epitopes of HSP70 (168-NVLRIINEPTAAAIA-18 and 389-QDLLLLDVAPLSLGL-403) were selected based on the immunoinformatics analysis. These epitopes showed high rates for inducing cytokines. The highest population coverage rates were 88.39% and 81.19% for CTL epitopes of HSP70285-298 and HSP70113-126, and 21.86% and 45.07% for HTL epitopes of HSP168-182 and HSP70389-403, respectively in the world's population.

Conclusion: The immunodominant, conserved, non-allergenic, non-toxic and immunogenic epitopes of HSP70 proteins were determined for design of a cancer vaccine construct.

Keywords: Innate immunity, Adaptive immunity, Heat shock protein, Immunoinformatics tools

Identification of key genes involved in Esophageal squamous cell carcinoma by bioinformatics analysis (Research Paper)

Sedigheh Sadat Mortazavi,[1] Zinat Shams ,[2] Roghayeh Sheervalilou,[3,*]

1. Division of Genetics, Department of Biology, Faculty of Sciences, Shahid Bahonar University of Kerman, Kerman, Iran.
2. Department of Biological Science, Kharazmi University, Tehran, Iran
3. Pharmacology Research Center, Zahedan University of Medical Sciences, Zahedan, Iran

Introduction: The commonest histological subtype of esophageal cancer, Esophageal squamous cell carcinoma (ESCC), is one of the deadliest human malignancies. Managing ESCC is still a challenge because of the late-stage diagnosis and metastasis. Also, despite recent advances in the therapy of ESCC, patients still develop therapy resistance and experience relapse. Therefore, this study aimed to improve the understanding of ESCC and investigate biomarkers for clinical management of its patients by comprehensive bioinformatics analysis.

Methods: In the present study, a microarray dataset containing gene expression data from ESCC patient samples was downloaded from the Gene Expression Omnibus (GEO) database. R software was applied to investigate differentially expressed genes in ESCC. Then, enrichment analyses were performed for the selected differentially expressed genes. Afterward, the protein-protein interaction (PPI) network was established using the Cytoscape software. Eventually, the top ten hub-genes were identified.

Results: There were 276 differentially expressed genes obtained from GSE161533 datasets. GO analysis results demonstrated that differentially expressed genes were mainly enriched in the extracellular matrix organization, collagen-containing extracellular matrix, and receptor ligand activity as the top terms of biological process (BP), cellular component (CC), and molecular function (MF), respectively. Moreover, the cytokine-cytokine receptor interaction was found as the significantly enriched pathway. Finally, ten genes, including MMP9, CXCL8, COL1A1, MMP3, POSTN, SPP1, MMP1, SERPINE1, COL1A2, and COL3A1, were identified as ten hub genes.

Conclusion: The findings of the present study suggest a list of genes applicable as novel diagnostic biomarkers and therapeutic targets for ESCC. Also, our results can support the application of public molecular data and computer-based approaches to develop more efficient strategies for the treatment of ESCC.

Keywords: Esophageal squamous cell carcinoma, biomarker, cancer

Identify Viruses With Their Mutations And Treat Them! (Research Paper)

Sajad Nouriposti,[1,*]

1.

Introduction: Abstract Learning about different types of viruses is very important today because of the prevalence of the unknown Coronavirus in today's world, this issue is even more important. Viruses have mutations that may be good or bad. The mutation rates of DNA viruses approximate those of eukaryotic. And the mutation of RNA viruses is higher. Viruses can create new organisms and species with their mutations, such as the Coronavirus in Brazil, which has created new species with its mutations. We need to prevent viruses from mutating so that new and more dangerous species are not produced than the previous virus. Viruses cannot be completely eradicated and directly destroyed, so it is vital for us to eradicate harmful viruses by producing vaccines. In this article, we understand that life is not possible without viruses. It should be noted that we can use other sciences such as physics to eliminate harmful viruses. In this world, we also have plant viruses that we must control. Failure to control them will lead to the destruction of all plants and consequently the destruction of the most important food source of humans. Viral mutations can produce new organisms, which can be very dangerous if we do not think about them. We will look at some of the ways to treat and combat viruses. This article is written just to get enough information about what has been said to make life a little easier in today's world of viruses.

Methods: 1Accurate Detection of Viruses 1.1. Types of viruses Today, we are witnessing the emergence of viruses in the world that have made scientists unsure of their previous and complete information about the types of viruses and continue to search for information about them. We look at most of the viruses that have been discovered to date. We have three categories of viruses. The first of them is Helical, the virus consists of nucleic acid enveloped by a hollow protein cylinder or capsid that has a helical shape, for instance, the Tobacco mosaic virus. . The second is the Envelope, the virus is covered with a modified section of the cell membrane, a protective lipid envelope, for example, Influenza and HIV. The third is Icosahedral, the virus is nearly spherical in shape, for example, most animal viruses. Viruses are composed of RNA or DNA and have a coat of protein, lipid (fat), or glycoprotein. Parasitic can not replicate without a host. They are the most abundant biological form of life on the planet and can not be cured, but a vaccination can prevent their spread. 1.2. The cost of deadly virus infections Over many centuries and even millennia, infection diseases such as smallpox and measles have claimed millions of lives. Advances in modern medicine have helped to stop the spread of many viral infections through mass

vaccination, and some infections have been completely eradicated. The Rabies virus has more than 100 rabies-related human deaths annually in the early 1900s and only one or two rabies-related human fatalities per year today. The virus of Measles was 120 cases in 2017 and before the vaccine developed in 1963, 3 to 4 million people were infected annually, resulting in 400 to 500 deaths each year. The Hepatitis virus new cases in 2017: hepatitis A: 3365. hepatitis B: 3409. hepatitis C: 4225. 5611 deaths in 2017. The Smallpox virus killed 3 in 10 infected individuals before a vaccine was developed and Eradicated in 1980 through vaccinations. The Chickenpox virus, in the early 1990s, 4 million people were infected annually, resulting in 100 to 150 deaths each year. The HIV virus, in 2017: 1.1 million Americans had HIV, 14% were unaware they had HIV and 38000 new HIV infections occur every year. The Flu virus: 55672 annual cases in 2017. 6515 annual deaths. The Poliovirus, in the 1940s, crippled more than 35000 people every year and caused more than 15000 cases of paralysis annually and no cases originating in the United States since 1979. The Coronavirus (Covid-19), declared a pandemic on March 12, 2020, by the World Health Organization (WHO). Most at risk: elderly individuals and those with underlying conditions 2. Mutations of Viruses 2.1. Mutation Rates and Outcomes The mutation rates of DNA viruses approximate those of eukaryotic cells, yielding in theory one mutant virus in several hundred to many thousand genome copies. RNA viruses have much higher mutation rates, perhaps one mutation per virus genome copy. Mutations can be deleterious, neutral, or occasionally favorable. Only mutations that do not interfere with essential virus functions can persist in a virus population. 2.2. Phenotypic Variation by Mutations Mutations can produce viruses with new antigenic determinants. The appearance of an antigenically novel virus through mutation is called antigenic drift. Antigenically altered viruses may be able to cause disease in previously resistant or immune hosts. 2.3. Vaccine Strains from Mutations Mutations can produce viruses with a reduced pathogenicity, altered host range, or altered target cell specificity but with intact antigenicity. Such viruses can sometimes be used as vaccine strains. 2.4. Mutations in Bacterial Viruses Genetic structure of viruses. It is interesting that so far the use of this method has only served to confirm inferences drawn from the study of patterns of spontaneous mutation. If it may be assumed that there is anything in common in the transformation of pneumococcal types (I), the fibroma-myxoma transformation (4), the induced mutations with respect to lysis-inhibition in bacterial viruses (Delbriick, this Symposium), it now appears for the first time that a biological phenomenon of general importance is involved. In the bacterial virus, three genetic factors chosen more or less at random for the test all appear to be transmissible from one viral particle to another. In view of the generality of this phenomenon, it will be surprising not to find that some counterpart to it already exists among the more familiar genetic mechanisms. Among the viruses, it is clear that it provides an additional mechanism for the production of new biotypes. 2.5. New viruses and species Researchers say all viruses

will mutate, and Corona is no exception. Most of the time, the change in the virus is either ineffective or increases its spread, or the new species gradually disappears, and in some cases, they may become more dangerous. Experts are currently focusing on a small number of new strains of the coronavirus: one strain in the United Kingdom that has become the dominant strain and spread to more than 50 other countries, one strain in South Africa in at least 20 other countries. Found, including in the UK, a new strain in Brazil. Professor Sharon Peacock, head of the British Genetic Surveillance Program, predicted that the coronavirus, first found in southeastern Kent, could become the dominant virus in the world. The coronavirus was first identified in September 2020 in southeastern Britain in the Kent area, and its rapid spread in the following months prompted the country to impose new restrictions. It is thought that English, South African, and Brazilian species may have a much higher rate of transmission than other types of the virus. The spike protein has been altered by all three types, the part of the virus that attaches to human cells. As a result, it seems that these species are more likely to infect and spread cells in the body. Mutations in coronavirus horn protein have caused concern because some vaccines are based on cloning. What are the characteristics of the new Kent virus? The Kent virus was first seen in southern Britain in September last year, mainly due to an increase in the number of positive coronary tests at the time in London, the southeast, and the east of England. Three factors drew attention to this new strain of the virus: It is rapidly replacing other types of viruses, It has mutations that affect the part of the virus that can be important and some of these mutations have already been shown in the laboratory to increase the virus' ability to infect cells. All of these factors give rise to a virus that can spread easily. However, experts say that so far there is no evidence that the virus is more dangerous. It was a year ago that the world became aware of the corona و virus, and the first cases of the disease were observed in a live animal market in Wuhan, China. Since then, the virus has had at least two mutations almost every month. If we compare today's virus with the original virus in Wuhan, China, they differ by at least 25 mutations. 2.6. How quickly do variants emerge? In fact, first, viruses have a mutation rate that's much, much higher than humans or other animals, and they replicate at a rate that's really, really fast. So in other words, one virus-infected cell makes 100,000 copies of itself, and all those copies can go out and start replicating. So mutations occur randomly, but because the virus replicates at such a fast rate, we also accumulate mutations really fast. But again, it's important to note that while mutations occur randomly, most of those mutations either do nothing to change how a virus behaves or they're detrimental. Over the first year of the pandemic, we saw a lot of these mutations popping up that were allowing us to track the virus. We could say that a certain mutation occurred in England in this month and that virus strain started to spread. And we could trace back where viruses came from based on these unique mutations, but none of them really changed the way the virus itself replicated. It's only now that we're getting into some of

these variants that are changing the way the virus behaves in the population. And again, that's just a really small set of all the mutations that accumulate in these viruses. 2.7. Is it possible to prevent a virus from mutating? Well, we can't prevent the virus from mutating, but what we can do is limit the virus's spread, and in that way, we reduce the chances that a mutation can emerge that is going to help the virus infect humans better. Say, for example, it's a one in a million chance that a mutation will be advantageous to the virus. If we let the virus replicate itself 900,000 times, odds are that the advantageous mutation will occur. But if we limit the overall replication of the virus to 1,000 times, then it's much less likely that the random advantageous mutation is going to occur. And that's where public health interventions really help us a lot during this pandemic—by reducing the total amount of virus replication and therefore reducing the chances that the virus can improve or adapt. 2.8. Impact of Pollution on Seasonal Respiratory Viruses Though meteorological data are regularly considered as influencing virus seasonality, there is much more debate about the importance of air pollution. Both indoor and outdoor air pollution may be important, and many of the same components (e.g., particulate matter (PM)) are found in both indoor and outdoor environments. Pollution variables have been studied more in relation to magnification and perturbation of seasonal disease than as causative agents. There is a body of research on the subject that is well-reviewed by Ciencewicki and Jaspers. Part of the problem with tying air pollution with infectious disease is that investigations of pollution have revealed conflicting results when looking at different cities, regions, and pollutants. The question as to whether air pollution itself shows seasonal variation is dependent on different pollutants and regions. SO2, for example, exhibits seasonality in the northern part of the United States, but not in the south. The most heavily investigated pollutants in relation to infectious disease epidemiology are ozone, SO2, NO2, and PM. The results of these studies are somewhat mixed depending on whether they are looking at human populations, animal models, or cell lines. High ozone is suggested to initiate inflammation in the lung. There have been associations found between ozone levels and hospital admissions for influenza and pneumonia, though studies with mice have produced results suggesting that the effect of ozone on infection depends on exposure time and duration. Ozone may actually reduce morbidity from influenza when exposure occurs after infection. Rhinovirus has been interestingly found to enhance the influence of ozone on the immune system, resulting in elevated levels of IL-8. The effect of PM on respiratory infection also seems to be linked to the immune response. Increased morbidity in mouse models of RSV have been found when they are exposed to fine black carbon. In several epidemiological studies, NO2 has been linked to increased infection susceptibility. Though untested, reinfection susceptibility, as well as susceptibility to initial infection, may be influenced by the effect of pollution on the immune system.61 The relationship between air pollution and seasonal virus transmission still leaves many questions, with conflicting studies as to the role of air pollutants on

respiratory viral transmission and morbidity. Though other influences may be more directly responsible for the phenomenon of seasonality, local or regional disparities may be influenced by air pollution levels that also vary with seasons. 2.9. Human Behavior and Socioeconomics Human seasonal behavior has often been cited as a strong reason for infectious disease seasonality. Examples of possible contributors include that individuals are indoors together more often during the winter and colder temperatures coincide with the beginning of the school year. Indeed these may serve to increase the disease incidence in a seasonally dependent way, though as has already been discussed, the human behavior theories are not currently considered primary causes. To make things even more complicated, it is possible that the factors associated with childhood and adulthood influenza epidemics may actually be separate. A study of transmission suggests that childhood influenza travels through the school system while adult influenza is spread more through work commuting and travel. Children are considered more socially connected than adults because of the school system and are therefore also suggested to be more susceptible to the first season of a new influenza. Therefore, epidemics within a single season or across multiple seasons can shift from children to adults as the more connected children develop immunity. There have been several studies of the association of individual risk factors, such as socioeconomic status, with risk of becoming infected. Most of these conclude that lower socioeconomic status increases risk of infection. Of course socioeconomic status itself is not causative, but rather factors associated with it such as smoking and lower vaccination in underserved populations combine to increase rates in these areas. On a local level, this may in fact be very important in determining how epidemics travel in the presence of favorable climatic factors. On a larger scale, human travel is important in the worldwide and nationwide diffusion of seasonal disease. Transportation hubs and more densely populated areas are more likely to serve as epidemic centers. California is frequently the source of the annual epidemic in the United States due to its high population and possibly because of the large volume of air traffic from the Pacific and to other areas of the country. New England states are usually affected later in the season. In simulations, epidemics that begin in areas with low populations spread slowly and sporadically. A seasonal epidemic beginning in California, however, exhibits very high synchrony that goes above and beyond what would be normally expected due to seasonal forces alone. 3. Viruses Can Help Us as Well as Harm Us As we learn more about the roles of viruses in the human virome, we may uncover more therapeutic possibilities. Alejandro Reyes of Washington University in St. Louis has shown that phages in mice can shape the rodents' bacterial communities, although we are not sure what changes first: the viruses or the bacteria. If the viral communities change first, they can sculpt the bacterial communities to serve them. If the bacterial communities change first, the viral communities are likely just adapting so they can infiltrate the reshaped bacteria. Researchers have shown that viromes can change

significantly in periodontal disease and in inflammatory bowel diseases. Although it will take a long time for us to unravel the human virome, it is important to consider how far we have come in just 10 years. A decade ago many scientists thought of the microbiome as a kind of passive layer of tiny organisms inside the body, mostly in the gut. Now we know that although some parts of the microbiome are indeed stable, some parts are active and changing. And it is beginning to look like the most dynamic players are the viruses. A 2018 study of brain tissue donated by people who had died of Alzheimer's disease revealed high levels of herpesviruses. Then, in May 2020, investigators at Tufts University and the Massachusetts Institute of Technology, who have developed brain-like tissue in the lab, infected their tissue with herpes simplex 1, and the tissue became full of amyloid plaque-like formations akin to those that riddle the brains of people who have Alzheimer's. It is startling to realize that we could discover remarkable roles for old viruses. As we look deeper, we may find new categories of viruses that impact human health, as well as new ways to exploit viruses to manipulate our microbiome and protect us from disease. If we humans can figure out how to manage the bad viruses and exploit the good ones, we could help ourselves become stronger superorganisms. 4. Ways to Boost our Immune System There are plenty of supplements and products in the grocery store that claim to help boost our immune system. But while it may sound like a no-brainer, boosting our immune system is actually much harder to accomplish than we might think — and for good reason. our immune system is incredibly complex. It has to be strong enough and sophisticated enough to fight off a variety of illnesses and infections, but not so strong that it overreacts unnecessarily — causing allergies and other autoimmune disorders to develop. To operate in such a delicate balance, our immune system is tightly controlled by a variety of inputs. But despite its complexity, there are everyday lifestyle habits we can focus on to help give our immune system what it needs to fight off an infection or illness. Here are five science-backed ways to ensure our immune system has everything it needs to function optimally, as well as why we shouldn't rely on supplements to boost our immune system. 4.1. Maintain a healthy diet As with most things in our body, a healthy diet is a key to a strong immune system. This means making sure we eat plenty of vegetables, fruits, legumes, whole grains, lean protein, and healthy fats. In addition to providing our immune system the energy it needs, a healthy diet can help ensure we're getting sufficient amounts of the micronutrients that play a role in maintaining our immune system, including: Vitamin B6, found in chicken, salmon, tuna, bananas, green vegetables, and potatoes (with the skin). Vitamin C, found in citrus fruit, including oranges and strawberries, as well as tomatoes, broccoli, and spinach. Vitamin E, found in almonds, sunflower and safflower oil, sunflower seeds, peanut butter, and spinach. Since experts believe that our body absorbs vitamins more efficiently from dietary sources, rather than supplements, the best way to support our immune system is to eat a well-balanced diet. 4.2. Exercise regularly Physical activity

isn't just for building muscles and helping ourselves de-stress — it's also an important part of being healthy and supporting a healthy immune system. One of the ways that exercise may improve immune function is by boosting our overall circulation, making it easier for immune cells and other infection-fighting molecules to travel more easily throughout our body. In fact, studies have shown that engaging in as little as 30 minutes of moderate-to-vigorous exercise every day helps stimulate our immune system. This means it's important to focus on staying active and getting regular exercise. 4.3. Hydrate Water plays many important roles in our body, including supporting our immune system. Fluid in our circulatory system called lymph, which carries important infection-fighting immune cells around our body, is largely made up of water. Being dehydrated slows down the movement of lymph, sometimes leading to an impaired immune system. Even if we're not exercising or sweating, we're constantly losing water through our breath, as well as through our urine and bowel movements. To help support your immune system, be sure we're replacing the water you lose with water we can use — which starts with knowing how much water you really need. 4.4. Get plenty of sleep Sleep certainly doesn't feel like an active process, but there are plenty of important activities happening in our body when we're not awake — even if we don't realize it. For instance, important infection-fighting molecules are created while we sleep. Studies have shown that people who don't get enough quality sleep are more prone to getting sick after exposure to viruses, such as those that cause the common cold. To give our immune system the best chance to fight off infection and illness, it's important to know how much sleep we should be getting every night, as well as the steps to take if our sleep is suffering. 4.5. Minimize stress Whether it comes on quick or builds over time, it's important to understand how stress affects our health — including the impact it has on our immune system. During a period of stress, particularly chronic stress that's frequent and long-lasting, our body responds by initiating stress response. This stress response, in turn, suppresses our immune system — increasing our chance of infection or illness. Stress is different for everyone, and how we relieve it is, too. Given the effect it can have on our health, it's important to know how to identify stress. And, whether it's deep breathing, mediation, prayer, or exercise, we should also get familiar with the activities that help us reduce stress. 4.6. One last word on supplements There's no shortage of supplements claiming they can stimulate our immune system — but be wary of these promises. First thing's first, there's no evidence that supplements actually help improve our immune system or our chances of fighting off an infection or illness. In addition, unlike medications, supplements aren't regulated or approved by the FDA. For instance, if we think a megadose of vitamin C can help us keep from getting sick, think again. If we're looking for ways to help boost our immune system, consider keeping up with the lifestyle habits above, rather than relying on claims on a label. 5. Ways to treat the virus 5.1. How can we treat viruses? There are a number of different methods that are available to treat certain viruses, for example,

viruses such as measles and polio can be prevented using a vaccine. There are also a variety of other treatments such as antivirals used to treat patients with HIV/AIDS and Hepatitis C. Despite this, the treatment of viral infections and the rise of antimicrobial resistance has proved a challenge, therefore the development of novel therapeutics and techniques to help prevent transmission and ease the risk of global outbreaks has had a pivotal role in the world of microbiology. Reducing the transmission of disease depends on which methods need to be engaged. Improving basic hygiene measures by washing your hands, keeping surfaces clean, and using a tissue to sneeze into, can all help prevent the spread of disease. Other factors, such as ensuring that communities have adequate access to safe drinking water and sanitation can also improve the risk of an outbreak. The threat of new and emerging diseases is still prevalent, as we have seen with the recent SARS-Cov-2 outbreak, alongside zoonotic diseases and arboviruses. In order to treat viruses, we need to engage in ongoing research in order to develop a better understanding of them. That way we will be in a position to respond rapidly to new and re-emerging viral diseases. 6. Plant viruses 6.1. Effective methods in controlling plant viruses Plant viruses cause considerable economic losses and are a threat for sustainable agriculture. The frequent emergence of new viral diseases is mainly due to international trade, climate change, and the ability of viruses for rapid evolution. Disease control is based on two strategies: i) immunization (genetic resistance obtained by plant breeding, plant transformation, cross-protection, or others), and ii) prophylaxis to restrain virus dispersion (using quarantine, certification, removal of infected plants, control of natural vectors, or other procedures). Disease management relies strongly on a fast and accurate identification of the causal agent. For known viruses, diagnosis consists in assigning a virus infecting a plant sample to a group of viruses sharing common characteristics, which is usually referred to as species. However, the specificity of diagnosis can also reach higher taxonomic levels, as genus or family, or lower levels, as strain or variant. Diagnostic procedures must be optimized for accuracy by detecting the maximum number of members within the group (sensitivity as the true positive rate) and distinguishing them from outgroup viruses (specificity as the true negative rate). This requires information on the genetic relationships within-group and with members of other groups. The influence of the genetic diversity of virus populations in diagnosis and disease management is well documented, but information on how to integrate the genetic diversity in the detection methods is still scarce. High-throughput or next-generation sequencing provides broad-spectrum and accurate identification of viruses enabling multiplex detection, quantification, and the discovery of new viruses. Likely, this technique will be the future standard in diagnostics as its cost will be dropping and becoming more affordable. 7. If all viruses disappeared, the world would be very different Viruses seem to exist solely to wreak havoc on society and bring suffering to humanity. They have cost untold lives over the millennia, often knocking out significant chunks of the global population – from

the 1918 influenza epidemic which killed 50 to 100 million people to the estimated 200 million who died from smallpox in the 20th Century alone. The current Covid-19 pandemic is just one in a series of ongoing and never-ending deadly viral assaults. If given the choice to magically wave a wand and cause all viruses to disappear, most people would probably jump at that opportunity, especially now. Yet this would be a deadly mistake – deadlier, in fact, than any virus could ever be. “If all viruses suddenly disappeared, the world would be a wonderful place for about a day and a half, and then we’d all die – that’s the bottom line,” says Tony Goldberg, an epidemiologist at the University of Wisconsin-Madison. “All the essential things they do in the world far outweigh the bad things.” The vast majority of viruses are not pathogenic to humans, and many play integral roles in propping up ecosystems. Others maintain the health of individual organisms – everything from fungi and plants to insects and humans. “We live in a balance, in a perfect equilibrium”, and viruses are a part of that, says Susana Lopez Charretón, a virologist at the National Autonomous University of Mexico. “I think we’d be done without viruses.” Most people are not aware of the role viruses play in supporting much of life on Earth, because we tend to focus only on the ones that cause humanity trouble. Nearly all virologists solely study pathogens; only recently have a few intrepid researchers begun investigating the viruses that keep us and the planet alive, rather than kill us. “It’s a small school of scientists who are trying to provide a fair and balanced view of the world of viruses, and to show that there are such things as good viruses,” Goldberg says. What scientists know for sure is that without viruses, life and the planet as we know it would cease to exist. And even if we wanted to, it would probably be impossible to annihilate every virus on Earth. But by imagining what the world would be like without viruses, we can better understand not only how integral they are to our survival, but also how much we still have to learn about them. 8. Using other sciences to kill viruses researchers are using tools from the field of physics and other scientific disciplines to help better understand COVID-19. In Hamburg scientists are studying the elusive protein structures that enable coronaviruses, including SARS-CoV-2, to take hold. They are trying to find out how they are able to replicate so rapidly inside human cells. 8.1. Producing proteins The more they know about these proteins, the better chance there will be to develop treatments and vaccines. The first step seeks to produce proteins in different cell types. Researchers say the challenge is huge. "The proteins have to be produced in different cell types and some proteins can resist this process, explains Boris Krichel, a virologist at Heinrich Pette Institute, adding: "That's always a little difficult. These proteins then become too large or are modified. This is why you have to take certain cell types in order to get them in a way they can be studied. Despite the obstacles, scientists say the work they are doing is crucial. “The job of these proteins is to replicate the viral genome. If we know how the individual parts function and how they are put together, then we can use this knowledge to develop drugs that specifically stop these individual proteins,” says Krichel.

"Ultraviolet lasers, mass spectrometry, protein structures, DNA, vaccine platforms. European researchers are leaving no stone unturned in the fight against COVID-19. Of course, this fundamental research gathers virologists, but it's also bringing together physicists, chemists, geneticists, and computer scientists, that could, according to many of them, soon start bearing fruit." 9. Who discovered the virus? The history of virology – the scientific study of viruses and the infections they cause – began in the closing years of the 19th century. Although Louis Pasteur and Edward Jenner developed the first vaccines to protect against viral infections, they did not know that viruses existed. The first evidence of the existence of viruses came from experiments with filters that had pores small enough to retain bacteria. In 1892, Dmitri Ivanovsky used one of these filters to show that sap from a diseased tobacco plant remained infectious to healthy tobacco plants despite having been filtered. Martinus Beijerinck called the filtered, infectious substance a "virus" and this discovery is considered to be the beginning of virology. The subsequent discovery and partial characterization of bacteriophages by Frederick Twort and Félix d'Herelle further catalyzed the field, and by the early 20th century many viruses had been discovered. In 1926, Thomas Milton Rivers defined viruses as obligate parasites. Viruses were demonstrated to be particles, rather than fluid, by Wendell Meredith Stanley, and the invention of the electron microscope in 1931 allowed their complex structures to be visualized.

Results: Results In the study, the types of viruses were examined in general and their types were fully described. Mutations in bacterial, RNA, and DNA viruses were also examined, and we found that new species of viruses may be produced using mutations. In the plant viruses mentioned, we found that the only way to deal with them is to control them, so we should not think about eliminating the viruses completely because we found that life without viruses is not possible. To reduce the effectiveness of viruses, we can strengthen our immune system and also use other science like physics to kill viruses, such as a number of scientists who are working hard in Hamburg. In this article, we could not find a cheap way to deal with viruses, because in the coming years, one of the most important human needs is a cheap way to deal with viruses. Also, we did not expect such a vast world of viruses and their processes, but we realized that the world of viruses is not only very large and vast, but human life would not be possible without them.

Conclusion: Conclusion Identify Viruses With Their Mutations And Treat Them makes us examine the world of viruses more carefully and realize their pros and cons so that we can think about their useful uses in the future. Have you ever wondered why we only think about the evils of viruses? Why did we never think that if there was no virus, we would not exist? These are questions we need to ask ourselves and answer in private. This research may be a very small part of other research in this field, but why has there not been

any discussion and analysis on the larger research in today's societies? All this is due to our insufficient knowledge of the world of viruses, which I hope this research can solve a small part of your ambiguities.

Keywords: virus, viral, mutations, other science, coronavirus, new species

Immunohistochemical expression of CB1 receptor in the liver of patients with HBV related-HCC (Research Paper)

Bita Moudi,[1,*] Zahra Heidari,[2] Hamidreza Mahmoudzadeh-Sagheb,[3] Mohammad- Reza Mohades,[4]

1. 1Infectious Diseases and Tropical Medicine Research Center, Resistant Tuberculosis Institute, Zahedan University of Medical Sciences, Zahedan, Iran
2. 1Infectious Diseases and Tropical Medicine Research Center, Resistant Tuberculosis Institute, Zahedan University of Medical Sciences, Zahedan, Iran
3. 1Infectious Diseases and Tropical Medicine Research Center, Resistant Tuberculosis Institute, Zahedan University of Medical Sciences, Zahedan, Iran
4. Department of Histology, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran

Introduction: The most common cause of HCC is HBV infection, which has a high death rate in the world. This study aimed to examine the immunoexpression of CB1 receptor in the liver of patients with HBV related-HCC in comparison with HCC, chronic HBV and healthy people

Methods: Participants in this case- control study were patients with only chronic hepatitis B (HBV=40), only hepatocellular carcinoma (HCC=41), HBV related-HCC (HBV + HCC=40) and healthy control group (C=30). Tissue expression of CB1 at the protein levels were studied using immunohistochemical method.

Results: All groups were statistically significant in terms of expression of CB1 protein ($p<0.001$). The expression levels of CB1 in liver tissue of HBV and C groups were not statistically significant ($p=0.072$). The expression level of CB1 in liver tissue of HBV related-HCC and HCC groups had a statistically significant increase compared to the C and HBV groups ($P<0.001$). Also, the CB1 expressions in liver tissues of HBV related-HCC and HCC groups were statistically significant ($P = 0.008$). Sensitivity and specificity of immunohistochemistry test in the diagnosis of HCC using CB1 were 63.4 and 91.2, respectively. Also, positive and negative predictive values were 90.0 and 65.1 %, respectively. There was no relationship between the expression of CB1and other clinicopathological variables ($p<0.05$).

Conclusion: The present findings reveal a tumor promoting function of the CB1 receptor in HCC. CB1 is also a pathological valuable factor in identifying the pathway of inflammation during infection.

Keywords: cannabinoid receptor type-1, HCC, HBV, immunohistochemistry.

Immunological and histopathological study on the effect of Ginseng extract and Ampicillin on endocarditis caused by Listeria monocytogenes (Research Paper)

Seyed Zanyar Athari,[1] Zahra Karamouz,[2] Mir Alireza Nourazar,[3] Yousef Doustar,[4] Younes Anzabi,[5,*]

1. PhD Student at Medical Physiology, Faculty of Medicine, Tabriz University of Medical Science, Tabriz, Iran.
2. Doctor of Veterinary Medicine, Faculty of Veterinary Medicine, Tabriz Branch, Islamic Azad University, Tabriz, Iran.
3. Department of Basic Sciences, Faculty of Veterinary Medicine, Tabriz Branch, Islamic Azad University, Tabriz, Iran.
4. Department of Pathobiology, Faculty of Veterinary Medicine, Tabriz Branch, Islamic Azad University, Tabriz, Iran.
5. Department of Pathobiology, Faculty of Veterinary Medicine, Tabriz Branch, Islamic Azad University, Tabriz, Iran.

Introduction: Endocarditis is a rare but serious infection caused by Listeria monocytogenes. Ginsan a polysaccharide extracted from Panax Ginseng demonstrated multiple immunomodulatory effects in earlier studies. Ampicillin is known as an effective antibiotic in the treatment of this disease. Therefore, this study aimed to evaluate the effect of hydroalcoholic extract of Ginseng and also ampicillin on endocarditis caused by experimental infection with Listeria monocytogeneses.

Methods: For this purpose 25 mice, 5-7 weeks, were randomly divided into five groups of 5 animals each including Healthy Control group, Infected group, Ampicillin (20 mg/kg-sc) treatment group, Ginseng (0.025 mg/kg-ip) Treatment group, and Ginseng (0.025mg/kg-ip)+Ampicillin (15mg/kg-sc) treatment group. At the end of the study, the concentration of murine cytokines in serum, such as IL-1 (Interleukine-1), IL-6, IL-8, and TNF-α was measured. Histopathological changes were evaluated in heart tissues.

Results: Serum levels of IL-1, IL-6, IL-8, and TNF-α were significantly decreased in the Ampicillin+Ginseng treated group in comparison with the other experimental groups $p<0.05$. Microscopically, pathologic changes in heart tissues were concomitant with biochemical findings.

Conclusion: This study showed that Ginseng hydroalcoholic extract plus Ampicillin has better efficacy than extract or antibiotic alone against experimental endocarditis caused by Listeriosis.

Keywords: Listeriosis, Cytokines, ELISA, Heart, Myocardial-edema

Impaired spermatogenesis caused by busulfan is partially ameliorated by treatment with conditioned medium of adipose tissue derived mesenchymal stem cells (Research Paper)

Amir Raoofi,[1,*]

1.

Introduction: Busulfan (BSU) is a chemotherapeutic drug that can cause subfertility or sterility in males. We investigated the effects of adipose tissue-derived mesenchymal stem cells (AT-MSC) conditioned medium (CM) (AT-MSC-CM) on histopathological and molecular characteristics of mouse testes exposed to BSU using stereology.

Methods: We used adult male mice divided randomly into five groups: control, Dulbecco's modified Eagle's medium (DMEM), dimethyl sulfoxide (DMSO), BSU, and BSU + CM. Thirty-five days following BSU injection, sperm and testis tissues were harvested for stereological and molecular studies.

Results: The BSU group exhibited significantly reduced testis volume, interstitium and tubules compared to the other groups, although the volume of the testis remained unchanged for BSU and CM groups. The number of testis cells was reduced in the BSU group compared to the other groups. The CM group exhibited a significantly increased number of testis cells compared to the BSU group. Sperm count and motility, and length density of seminiferous tubules were increased in CM group compared to the BSU group.

Conclusion: We observed beneficial effects of AT-MSC-CM on spermatogenesis and other cells of testes exposed to BSU. AT-MSC-CM exhibited regenerative properties for treating histopathologic changes of mouse testes exposed to BSU. AT-MSC-CM may be useful for therapeutic purposes and research concerning testicular infertility.

Keywords: Adipose tissue; azoospermia; busulfan; conditioned medium; mesenchymal stem cells; mice; spermatogen

Implementation of Chimeric Antigen Receptor T Cell Therapy in Cancer (Review)

Kimia Asghari,[1,*]

1. university of Isfahan

Introduction: Chimeric antigen receptor T-cell therapy (CAR T-cell) offers a new treatment option for patients with diffuse large B-cell lymphomas and acute lymphoblastic leukemia (ALL), both aggressive forms of blood cancer. CAR T cells are patient-modified T cells that are genetically engineered to target a cancerous cell's surface antigen with their synthetic receptors, which reprogram T cells to fight cancer. In this way, the immune system targets cancerous cells and increases the effectiveness of cancer therapies. The CAR is the central component of CAR-T cells, forming T cells major histocompatibility complex (MHC) unrestricted. Modified T cells can recognize a broader range of targets than natural TCR molecules on T cell surfaces. CARs are recombinant receptors that can bind to tumor antigens and activate T cells at the same time. The CAR consists of three distinct parts, each with a different task. An extracellular domain is a single-chain variable antibody domain (scFv), that is able to recognize specific antigens of tumors. A small segment of polypeptide connects the heavy-chain variable region (VH) to the light-chain variable region (VL) of antibodies. The scFv on CAR-T cells allows them to recognize and bind directly to tumor-specific antigens. The hinge domain consists of members of the immunoglobulin superfamily, such as CD8, CD28, or IgG, which are involved in signal transduction. Signal transduction within the intracellular space is primarily due to the TCR CD3ζ chain. CAR-T cells identify tumor surfaces antigens directly and they are not limited by MHC class. In response to this binding, CAR-T cells multiply and destroy tumor cells. Initially, CAR T cells have been used to treat malignancies that express the CD19 antigen, such as lymphoma and ALL. Moreover, CAR T cells can target other targets, including overexpressed antigens, such as epidermal growth factor receptor (EGFR) and human epidermal growth factor receptor 2 (HER2), glycosylated abnormal proteins such as mucin 1 (MUC1), oncofetal antigens such as carcinoembryonic antigen (CEA), tumor-associated stromal proteins such as fibroblast activating protein (FAP) and immune-modulating antigens such as program death-ligand 1 (PD-L1). TCR-T cells can recognize any antigen presented by MHC molecules, whether they are intracellular or surface antigens or neoantigens produced by tumor cells after mutation, and also TCR can recognize the internal molecules of cancer cells. When a small amount of antigen is present, TCR-T cells can be fully activated because they retain all the auxiliary molecules of the TCR signal transduction pathway. There are several side effects associated with CAR T cells that are related to the way they attack cancer cells in All patients. Often, patients suffer from cytokine release

syndrome (CRS) due to excessive T-cell activation. Symptoms of CRS can include high fever, hypotension, hypoxia, and even organ failure. Inflammatory cytokines such as IL-6, IFNγ, and TNFα are responsible for these symptoms. A longer-term side effect can also happen due to the normal expression of the CD19 protein on normal B cells, which are a type of white blood cell that functions as part of the immune system by releasing antibodies. As a result of the treatment, patients can have low levels of antibody production and become more susceptible to infection.

Methods: CAR T-cell therapy involves genetically editing a patient's T-cells to express a CAR that recognizes an antigen-specific to his or her tumor, followed by ex vivo cell expansion and re-infusion back into the patient. T-cell genetic modification may take place either via viral-based gene transfer methods or nonviral methods.

Results: A genetically manipulated CAR T cell can target specific cancer cells; it has been successfully used in research facilities to treat solid and suspended cancers. This method uses the patient's own peripheral blood mononuclear cells and after some special experiments, these modified T cells can recognize and bind to specific antigens on cancer cells and destroy them.

Conclusion: It has been shown that CAR-T cells are an effective and promising treatment for cancer but they also faced many challenges. The CAR-T cell therapy is simply the beginning of immunotherapy, not the end. In addition, future treatment schemes must combine immunotherapy with other methods.

Keywords: Cancer, immunotherapy, T-cell therapy, chimeric antigen receptor (CAR-T), CD19-targeted CAR-modified

Improvement of the proliferation and stemness of human hair follicle stem cells via low level laser irradiation (Research Paper)

Mina Sadat Naderi,[1] Seyed Mehdi Tabaie,[2,*]

1. Assistance Professor, PhD of Biophysics, Department of Biophysics, Faculty of Biological Sciences, Islamic Azad University, Tehran North Branch ,Tehran, IRAN
2. MD, Dermatologist, Associated Professor, Department of Medical Laser, Medical Laser Research Center, Yara Institute, ACECR, Tehran, IRAN

Introduction: Low level lasers are currently used for many medical applications, including wound healing as well as hair loss treatment. Hair follicle stem cells (HFSCs) are used as a model for the primary skin papilla cell system. HFSCs are attractive candidates for clinical repair and regenerative medicine. The methods that augment the stemness characteristics improved applications of stem cells. Low level laser radiation can stimulate cell proliferation. In some studies, the effect of low level laser has been investigated for the treatment of androgenic alopecia. It should be noted that low level laser can increase cell proliferation by affecting the NF-κB pathway.

Methods: In this study, the effect of low level laser irradiation on the proliferation and stemness gene of human hair follicle stem cells were investigated. At first, hair follicle stem cells were extracted by enzymatic and mechanical methods, and then confirmation tests of hair follicle stem cells were performed by flow cytometry. After the laser power meter, the potential of the low level laser with the energy density of 1 and 5 J/cm2 as a treatment on the proliferation and also expression of stemness genes such as Sox2, Oct4 and Slug was investigated.

Results: The result of this study indicate that the low level laser irradiation increase the proliferation of HFSCs under the 5 J/cm2 irradiation. Expression of stemness genes (Sox2, Oct4 and Slug) also increase. low level laser irradiation not only can be preventing the decrement of the stemness characterized but also increase the expression of stemness genes of the hair follicle stem cells.

Conclusion: This result paves the way for utilizing the hair follicle stem cells for effective applications in cell therapy and wound healing.

Keywords: hair follicle Stem cells, Low level laser, Stemness

Improving the quality of IVF as an assisted reproductive technology: by enriching the culture medium (Review)

Zeinab Bahrami,[1] Mahmood Talkhabi,[2,*] Rouhollah Fathi,[3]

1. Department of Animal Sciences and Marine Biology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
2. Department of Animal Sciences and Marine Biology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
3. 2Department of Embryology, Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, Academic Center for Education, Culture and Research (ACECR), Tehran, Iran

Introduction: Infertility, as a problem with different causes, forces millions of people to take clinical proceedings to solve this problem every year. Researchers are always looking for new ways to increase the efficiency and effectiveness of clinical infertility treatments. In Vitro Fertilization (IVF) is a complex series of procedures used to help with fertility or prevent genetic problems to have a offspring. During IVF, after stimulating ovulation with the use of drugs, the oocytes are collected and fertilized in vitro,with sperm. It should be noted that in vitro culture, although it tries to be suitable and similar to in-vivo, but due to the lack of signaling and molecular pathways in the body and the inevitable difference in physicochemical conditions, destructive effects on the embryos. To solve the existing problems, researchers have used various compounds as supplements in the process of embryo growth and development invitro. To this end, researchers have found useful results in finding ways to make in-vitro conditions more similar to the in-vivo . Adding different supplements to culture media to improve the conditions of fertilization can be considered in line with these efforts. In this article, we review the published research with the approach of examining the effects of different supplements on IVF and embryo culture.

Methods: In this article, we provides an overview recent studies in improving the quality of embryos grown in enriched culture media with various supplements. We fouced on the effect amino acids ,Cytokines, hormones in embryo culture media and sperm capacitation media. The quality of embryos in experimental groups at different stages of development including two cells, cleavage and blastocyst was examined. The present review article is the result of a review of 58 studies from 2017 to 2020 in this field and among English language articles.

Results: This study showed that the use of supplements, which are generally present invivo situation, in the laboratory, can help increase the rate of embryo formation, blastocyst formation, and ultimately increase live birth. the addition of the arginine to the sperm capacitation medium was effective in

improving sperm capacitation by increasing NO production. The addition of interleukin 6, as a single embryo-secreted factor, to the culture medium in vitro, helps to increase embryo growth. The use of 4-Hydroxy estrogen (4-OH-E ,a steroid production) along with EGF and PRL (prolactin) helps to increase the blastocyst implantation rate. In addition, the use of melatonin as a hormone helps to break down cell blocks in the embryo.

Conclusion: Our review study showed the addition of effective compounds that are also present in-vivo situation, such as amino acids (arginine), cytokines (interleukin 6), hormones (melatonin) and steroids(4-Hydroxy estrogen) to the culture medium in vitro can improve embryo quality and ultimately increase fertility in infertile cases.

Keywords: IVF, conditioned media,supplement,blastocyst,infertility

In silico screening and ADMET Studies of natural potential inhibitors against Myeloperoxidase from Cucumis melo L. Seeds with antioxidant and anti-inflammatory effects (Research Paper)

Mohammadreza Forouharmanesh,[1,*] hossin ameri shahrabi,[2]

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Introduction: Circulating neutrophils, monocytes and some tissue macrophages expressed Myeloperoxidase (MPO) a haem peroxidase-cyclooxygenase enzyme with vital antimicrobial and antiviral role by oxidizing halide and pseudohalide ions by H2O2. MPO-derived oxidants as a consequence of MPO discharging outside the phagocytes, lead to cardiovascular diseases, inflammatory diseases, neurodegenerative diseases, kidney diseases, and immune-mediated diseases. Therefore, MPO presents a critical target for design and development of inhibitors with therapeutic effects for these diseases. Medicinal plant-based compounds with great enzyme inhibitory effects have potential to investigate for drug design. Cucurbitaceae family members like Cucumis melo L. are proposed as highly valuable fruits serve as nutrition or medicine. The seeds of melon as by-products or waste contain phenolic compounds with potential antioxidant and anti-inflammatory properties. These natural inhibitors have great potency to develop as therapeutic agents for cancer or inflammatory diseases. In the current study, the activity of 6 natural compounds in seeds of melon as MPO potential inhibitor was analyzed by in silico studies.

Methods: The x-ray crystallography structure of human MPO with 5FIW PDB ID was obtained from RCSB PDB (https://rcsb.org) for in silico studies. PrankWeb (http://prankweb.cz/) was used for predicting and visualizing the ligand binding site of MPO. For ligand preparation, first, the chemical structures of natural compounds from seeds of melon were retrieved from PubChem compound database, following their structures were prepared by ChemBioDraw, and then PyRx tool converted the MOL SDF format to PDBQT file. Then, MPO as a receptor enzyme and natural phenolic compounds as ligands were prepared for molecular docking. The molecular docking was done using AutoDock 4.2.6 with the help of AutoGrid for the grids computation and AutoDockTools (ADT) for docking run and analysis. Then, the 3D structures of MPO-natural compounds generated by molecular docking were analyzed by further computational investigations. LIGPLOT v.4.5.3 was used to generate 2D schematic diagrams of MPO-natural compounds interactions to study the protein-ligand interactions map. Absorption, distribution, metabolism, excretion and toxicity (ADMET) parameters of natural compounds including physicochemical descriptors, pharmacokinetics properties, and the druglikeness were evaluated by ADMETlab 2.0

(https://admetmesh.scbdd.com/) and SwissADME (http://www.swissadme.ch/). Also, eMolTox webserver (http://xundrug.cn/moltox) was utilized for the prediction of potential toxicity of our investigated compounds by machine learning methods.

Results: From literature search, we selected 6 natural compounds including ellagic acid, catechin, quercetin, vanillin, eugenol, and caffeic acid extracted from Cucumis melo L. seeds as potential MPO inhibitors with phenolic property for in silico screening and ADMET analysis. First, PrankWeb predicted the critical residues of MPO in ligand binding site. These leading residues were used for obtaining site specific molecular docking results. All these phenolic compounds form Cucumis melo L. seeds showed great docking results with binding energy between -4.9 to -7.2 kcal/mol. Molecular docking results showed that among these 6 natural compounds catechin with the lowest binding energy (-7.2 kcal/mol) showed the higher binding affinity and a proper binding pose in MPO ligand binding site. 2D maps generated by LIGPLOT revealed that the hydrogen bonds played essential roles in MPO-natural compounds interactions. The predicted ADMET parameters for these phenolic compounds like solubility, LogD, LogP were acceptable with no mutagenic and carcinogenic effects. All these compounds were predicted as non-toxic by eMolTox web-server

Conclusion: Our in silico screening and ADMET analysis showed the potency of plant-based natural compounds from Cucumis melo L. seeds with antioxidant and anti-inflammatory properties to act as new MPO inhibitors with high affinity to MPO binding site, no toxicity, and acceptable ADMET parameters. This computational analysis needs more computational and experimental studies for development of new therapeutic agents for cancers or inflammatory diseases.

Keywords: Myeloperoxidase, Cucumis melo L., Natural inhibitor, ADMET, Drug design

In vivo Evaluation of bone regeneration behavior of macroporous β-TCP/layered double hydroxide nanocomposite granule-shaped bone substitute (Research Paper)

Neda Eskandari,[1,*] Seyedeh Sara Shafiei,[2] Mohammad Mehdi Dehghan,[3]

1. Department of Stem cell and Regenerative Medicine, Institute of Medical Biotechnology, National Institute of Genetic Engineering and Biotechnology, Tehran 14965/161, Iran
2. Department of Stem cell and Regenerative Medicine, Institute of Medical Biotechnology, National Institute of Genetic Engineering and Biotechnology, Tehran 14965/161, Iran
3. Department of Surgery and Radiology, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran

Introduction: Large bone defects in the trauma, tumor or congenital deformity represent a difficult problem in orthopedic surgery. Bone defects are often too large to be fixed by self-healing, so it can lead to the bone deformation. Many experiments have demonstrated that calcium phosphate ceramics can be easily fabricated and they have unique physical and chemical properties. The suitable biomaterial alternatives for potential bone regeneration is β-tricalcium phosphate (β-TCP). Porous β-TCP granules are clinically used in maxillofacial surgeries and implants fixation but its biomedical applications have been largely limited by their poor mechanical properties. One strategy to overcome this challenge is to design calcium phosphate-based nanocomposites. Several studies have demonstrated that the mechanical strength of CaP materials can be improved by using a suitable reinforcing phase such as biocompatible nanoparticles. Layered Double Hydroxides (LDHs; with the formula Mg6Al2(OH)16CO3·4H2O), also called anionic nanoclays, are clay-like materials that show promising properties for a large number of applications. Recently, researchers have reported the use of LDH nanoparticles as reinforcing agents of polymeric matrices. The addition of LDH to CaPs may modify physicochemical, mechanical and biological properties of CaPs. In our previous study, for the first time, we showed that the inclusion of LDH into β-TCP granules enhanced mechanical properties of β-TCP. The mechanical test proved that the inclusion of LDH nanoclay into β-TCP granules caused an increase in compressive modulus that make it suitable for load bearing areas of bone structure, thus reducing the risk of bone fractures that is an important issues commonly reported. This study was based on in vivo assessment of bone regeneration capacity of synthesized porous β-TCP/LDH nanocomposite granules. The aim of this study was to explore the effects of β-TCP granules reinforced with LDH compared to pristine β-TCP granules, in terms of osteoconductivity and biodegradability.

Methods: For the in vivo investigation of the porous granules, we used a total of 18 male New Zealand white rabbits. Three non-critical defects were produced on the distal femur by a dental drill. Then, defects were filled with the two different types of granules (with/without LDH) and the bone defect without any treatment was used as the negative control and were left in situ for up to 3 months for evaluation of bone neoformation. In this study, X-ray radiographic, micro-computed tomography and histological staining analysis were taken to evaluate the percentage of bone ingrowth and biodegradability of the porous granules.

Results: After 12 weeks of the implantation, the results indicated that in the empty defect, there was only 6.5% new bone formation, whereas in the defected filled with β-TCP granules, there was 33.3% new bone formation and 33.3% granule residues, Also, the defected filled with β-TCP/LDH granules showed the powerful capability of 40% bone regeneration and 46.6% granule residues in 3 months, Which implies that most of the porous β-TCP in bone defect areas was absorbed and bone regeneration increased critically in both of β-TCP granules during the study and also the amount of new bone formation in the bone defect filled with both of granules was almost six times higher than the empty defects. Although no significant difference in bone formation for two different granules was observed, the higher biodegradability was detected in β-TCP granules in comparison to β-TCP/LDH granules. It can be concluded that the osteoconductity properties have been preserved and its biodegradation rate has been decreased by addition of LDH.

Conclusion: It can be deduced that the bone defects regenerated with the both of β-TCP granules become similar to the non-manipulated bone and the both of β-TCP granules were biodegradable, which is essential property for bone regeneration and the composite of β-TCP granules with LDH were effective in inducing the bone formation. As the granule residues in β-TCP/LDH granules was higher than β-TCP granules, so the degradation rate was slower in this novel nanocomposite, we can consider it a good point that this nanocomposite could prevent osteoporosis by reducing osteoclasts reabsorption and brings the advantage of bone mechanical stability for load-bearing sites of the skeleton and reduces the risk of bone fracture. Therefore, it seems that the β-TCP/LDH nanocomposite granules has the potential to be a good candidate for orthopedic or reconstructive surgery.

Keywords: regeneration-granules -biodegradability- defects-calcium phosphate ceramics

In-vitro development of germ cell-like cells derived from human theca stem cells in reaggregated ovary (Research Paper)

Seyedeh Nasim Mirbahari,[1] Azam Dalman,[2,*] Fatemeh Hasani,[3] Mehdi Totonchi,[4]

1. Department of Embryology, Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran
2. Department of Embryology, Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran
3. Department of Embryology, Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran
4. Department of Genetics, Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran

Introduction: In this study, human theca stem cells (hTSCs) were differentiated into human germ cell-like cells (hGCLCs) and the developmental potential of these cells was measured after being placed next to somatic cells in reaggregated ovary.

Methods: In this interventional experimental study, hTSCs were isolated from small antral follicles (3-5 mm in size). Isolated hTSCs were expanded and seeded in 6-well plates at a density of 5×104 cells/well in differentiation medium (DMEM-F12 containing 5% human follicular fluid and 5% FBS) for 40 days. The hGCLCs aggregated with somatic cells (cumulus cells and hTSCs) in ratio of 1 to 5 and cultured in growth medium (αMEM containing 3mg/ml BSA, 1% ITS, 0.005 IU/ml FSH and 0.11 mg/ml ascorbic acid) in suspension culture dish for 10 days. The size, morphology, viability and the expression of oogonial-specific marker (DAZL) and oocyte-specific markers (GDF9) in hTSCs, hGCLCs and reaggregated ovaries were evaluated by immunostaining to assess the development process.

Results: The morphology of hTSCs changed to round-shape cells (hGCLCs), similar to oocytes, after 12 days (size 20µm) and the diameters of these cells increased over time (50µm, $P<0.05$). The viability of hGCLCs cells after in vitro differentiation and development in reaggregated ovaries was 54%. The hTSCs did not express DAZL and GDF9, but the hGCLCs expressed DAZL marker, and did not express GDF9. The hGCLCs expressed GDF9 after being placed in reaggregated ovary.

Conclusion: To sum up, hTSCs have the ability to differentiate in to hGCLCs in-vitro. In addition, morphological similarities and protein presence imply that in-vitro hGCLCs development improved by co-culturing with ovarian somatic cells.

Keywords: Theca stem cell, Differentiation, Reaggregated ovary, Germ cell like cells, cumulus cells

Induction of apoptosis by galectin-9 in LNCaP cell line of prostate cancer (Research Paper)

Narges Zargar Balajam,[1,*]

1. Department of Clinical Biochemistry, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences. Isfahan, Iran.

Introduction: Galectin-9, as a member of the lectin family with a beta-galactoside recognition domain, plays a significant role in inhibiting tumor cell proliferation. Prostate cancer is the second most common cancer in men and the sixth leading cause of death worldwide. In this study the effect of galectin-9 was investigated in LNCaP cell line of prostate cancer.

Methods: MTT viability test was applied to study the cell proliferation effect of galectin-9 in LNCaP cell line with various concentrations of galetin-9. Detection of apoptosis was conducted using the Annexin V-FITC/PI method.

Results: Our results showed that galectin-9 significantly reduced Cell viability in a dose-dependent manner ($P< 0.5$). In addition, further analysis showed that this growth inhibition was related to apoptosis induction by galactine-9 in the LNCaP cell line.

Conclusion: In conclusion this study demonstrated that galectin-9 can inhibit cell proliferation and induce apoptosis in the LNCaP cell line. Thus, the inhibition of galectin-9 in tumor cells may be potentially a target in prostate cancer that needs to be explored in future.

Keywords: Galectin-9, Prostate Cancer, Apoptosis

Injectable platelet rich fibrin (i-PRF) bioscaffold improves total antioxidant capacity in mouse transplanted ovarian tissue (Research Paper)

Sahar Hatami,[1,*] Seyed Mohammadali Shariatzadeh,[2] Malek Soleimani Mehranjani,[3]

1. Phd student, Department of Biology, Faculty of Science, Arak University
2. Department of Biology, Faculty of Science, Arak University
3. Department of Biology, Faculty of Science, Arak University

Introduction: However, Ovarian tissue transplantation can be a promising solution for preserve fertility return in cancerous women and girls. But, ischemia-reperfusion (I/R) injury occurs during the early post-transplantation days leads to oxidative stress and reduction graft function and long-term survival of the transplanted organ. Injectable platelet rich fibrin (i-PRF) is a liquid formulation of platelet rich fibrin (PRF) without the use of anti-coagulants. i-PRF is bioscaffold that contains leukocytes, circulating stem cells, platelets and growth factors. In the present study, we investigated the effect of i-PRF bioscaffold on the serum level of malondialdehyde (MDA) and total antioxidant capacity (TAC) after mouse ovarian tissue transplantation.

Methods: 18 Mice were randomly divided into three groups): control, autograft + saline (whole ovarian tissue transplanted in the gluteus superficialis muscle, saline directly injected into it), autograft + i-PRF (whole ovarian tissue transplanted in the gluteus superficialis muscle, i-PRF was directly injected into it). Serum concentrations of MDA and TAC were measured 7 days after ovary transplantation. Data were analyzed using one-way ANOVA and Tuckey's test and the means were considered significantly different at p-value < 0.05.

Results: In the autograft group, Serum concentrations MDA significantly increased in compare to the control, while it showed a significant decrease in the autograft + i-PRF group compared to the autograft group ($p < 0.05$). Moreover, the serum level of TAC decreased significantly in the autograft group compared to the control counterpart, whereas it increased significantly in the autograft + i-PRF group compared to the autograft group ($p < 0.05$).

Conclusion: These data showed that i-PRF bioscaffold at the graft site can decrease stress oxidative. therefore can prevent IRI injury through increasing total antioxidant capacity.

Keywords: Ovarian tissue transplantation, Injectable platelet rich fibrin (i-PRF), Ischemia–reperfusion, Stres

Integrative analysis of DNA methylation and gene expression to identify clear cell renal cell carcinoma diagnostic biomarkers via a machine learning approach (Research Paper)

Maryam Sadat Hosseini,[1] Parvaneh Nikpour,[2,*]

1. Department of Genetics and Molecular Biology, Isfahan University of Medical Sciences, Isfahan, Iran
2. Department of Genetics and Molecular Biology, Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

Introduction: Kidney tumors are responsible for 2.2% of all cancer diagnoses around the world each year. Approximately 70% of malignant kidney tumors are clear cell renal cell carcinoma (ccRCC). Because of ccRCC's obscure initial symptoms, most patients are diagnosed in a late stage and this clears the need for biomarkers that can help for its early detection. In the current study, our purpose is to integrate methylation and gene expression data from The Cancer Genome Atlas (TCGA) to find potential diagnostic biomarkers for ccRCC via bioinformatics and a machine learning approach.

Methods: Study population: DNA Methylation and gene expression data for KIRC project (Kidney renal clear cell carcinoma) were downloaded from TCGA using TCGABiolinks package in R. For DNA methylation, we obtained 160 normal and 324 tumor samples based on Illumina Infinium Human Methylation 450 platform. lluminaHiSeq RNASeqV2 gene expression data for 72 normal and 533 tumor samples was used for expression analysis. Differential methylation and expression analyses: At first, probes locating at sex chromosomes, containing SNPs or missing values were removed. We used ChAMP package for finding differentially methylated CpGs (DMCs). CpGs with adjusted p-values<0.05 and |delta β| > 0.15 were considered DMCs. IlluminaHumanMethylation450kanno.ilmn12. hg19 package was used for annotating methylation probes. Gene expression dataset was normalized via DESeq2 package. Genes were considered differentially expressed (DEGs) if they satisfied the threshold of |log2-based fold change| > 1 and adjusted p-values<0.05. Protein–protein interaction (PPI) network: Search Tool for the Retrieval of Interacting Genes (STRING) was used to create a PPI network with interaction score of 0.4. MCODE was used to pull out modules of the PPI network. Top two modules were analyzed using CytoHubba app in Cytoscape. Screening of diagnostic biomarkers via machine learning: Recursive feature elimination (RFE) method was used to choose top three genes from those which were selected by CytoHubba. These three genes where then used for constructing a logistic regression model.

Results: Since the promoter methylation has a great impact on gene expression, we only looked for DMCs which were mapped to promoter of the

genes, so 1400 CpGs were selected. Then we mapped these DMCs to genes and identified 874 non-duplicated genes which their promoter methylation level is significantly different in tumor and normal samples. For expression data, after normalization, a total of 5826 DEGs were found. Next step was intersecting between those 874 differentially methylated genes and 5826 DEGs. After intersection, we ended up with 303 genes that we used for construction of a PPI network. MCODE was applied for module analysis of network and top two modules were selected for downstream analysis with cytoHubba. On each module, we chose top 15 genes based on 3 criteria (degree, betweenness and closeness). Then to determine reliable ccRCC biomarkers, we intersected these 3 lists to find the common top genes which where 6 ones on each module. We imported expression data of these 12 genes to scikit-learn library in python. After feature selection with RFE method, 3 genes including CENPM, GAPDH and LAPTM5 were selected. We split the data to 30% test and 70% training and built a diagnostic logistic regression model with 3 selected genes with training samples. Accuracy of model performance on the test data was 96% indicating that the three markers could achieve excellent performance in distinguishing KIRC tumor and normal samples.

Conclusion: In this study, we analyzed DNA methylation and gene expression profiles in ccRCC samples from TCGA and came up with 3 genes that can discriminate tumor and normal samples with 96% accuracy. Several studies have shown LAPTM5 plays a role in development of different types of cancers. For example, it has great impact on proliferation of bladder cancer cells via G0/G1 phase. GAPDH can impact metastasis in renal cancer. It also has impact on the pathogenesis of cancer via regulation of autophagy and apoptosis. CENPM facilitates tumor metastasis in pancreatic cancer via mTOR/p70S6K signaling pathway. It also impacts invasion of cancer cells in hepatocellular carcinoma. In conclusion, since these markers are passed through multiple filters and because machine learning approaches are very effective for building diagnostic models, these markers could be helpful for early detection of ccRCC.

Keywords: Machine learning, Clear cell renal cell carcinoma, Diagnosis ،DNA methylation, Gene expression

Interleukin-17A and 17F mRNAs expression patterns change in COVID-19 Patients (Research Paper)

zeynab rahni,[1,*] Seyed Reza Mohebbi,[2] Seyed Masoud Hosseini,[3] Shabnam Kazemian,[4] Mahsa Saeedi Niasar,[5] Hamid Asadzadeh-Aghdaei,[6]

1.
2. Research Center for Gastroenterology and Liver Diseases, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
4. Research Center for Gastroenterology and Liver Diseases, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
5. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
6. Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Introduction: The severe outbreak of coronavirus 2019 (COVID-19), induced by the acute respiratory syndrome-coronavirus 2 (SARS-CoV-2), caused an exceptional public health crisis worldwide. Novel findings revealed that SARS-CoV-2-induced hyperinflammatory clinical condition contributes to disease complexity and fatality in COVID-19. Clinical studies in Covid-19 patients have shown that upregulation of cytokines and interferons in SARS-CoV2-induced pneumonia is associated with cytokine storm syndrome. Effective cytokines in cytokine storms include IL-6, IL-1β, IL-10, TNF, GM-CSF, IP-10, IL-17, MCP-3. In the blood of severe cases of COVID-19, large numbers of CCR4+ / CCR6+ Th17 cells can have high proinflammatory effects that support the Th17 cytokine storm. The Th17-type cytokine storm, which is associated with a dramatic increase in the cytokines IL-17, TNF, and GM-CSF, may result in organ damage Usually seen in severe COVID-19 patients. The aim of this study was to evaluate the expression of cytokine IL-17A and IL-17F in the blood of COVID-19 patients compared to the healthy control group.

Methods: The total RNA was extracted from the blood of the 20 COVID-19 patients and 20 healthy control subjects. Participants in this study were 13 male and 7 female in the patient group and healthy control group were 12 male and 6 female. qRT-PCR was performed to quantify the expression profile of IL-17A and IL-17F in blood of patients and control groups using the SYBR Green approach.

Results: The relative expression levels of IL-17A and IL-17F significantly increased in COVID-19 patients compared to the normal group (fold change: 4.217 ± 0.4768 $p < 0.0001$, 5.267 ± 0.5122 $p < 0.0001$ respectively).

Conclusion: Our findings demonstrate that the mean expression level of IL-17A and IL-17F genes are significantly increased in the infected patients with SARS-CoV-2 compared to the healthy group.

Keywords: COVID-19, cytokine, Interleukin-17A, Interleukin-17F

Interventions affecting the sexual self-concept: A Scoping review (Review)

fateme seyri,[1,*] dr soghra khani,[2]

1. Mazandaran University of Medical Sciences
2.

Introduction: Sexual self-concept is one of the parts of self-concept in human beings that refers to women's attitudes, beliefs and feelings about the organs and genitals that are involved in sexual intercourse. On the other hand, sexual intercourse is a means of uniting couples. Considering the importance of sexual issues in strengthening the foundation of the family and especially the importance of the sexual self-concept component, this study was conducted with the aim of reviewing interventions that promote women's sexual self-concept.

Methods: Search in 8 electronic databases and one search engine was performed from 10/02/1400 to 10/03/1400. 13 articles matched the inclusion and exclusion criteria and formed the final sample. They Were classified into 4 categories.

Results: In the first category, which included education (education to acquire sexual expression skills, education of sexual issues to women on the verge of marriage, genital anatomy knowledge film, QOLT(quality of life therapy), had an effect but education with package had no effect. On the second floor, rhinoplasty did not affect sexual self-concept, but genital cosmetic surgery did. On the third floor, lifestyle changes, and on the fourth floor, counseling interventions improved sexual self-concept.

Conclusion: According to the contradictory results, more interventions are needed to improve women's sexual self-concept.

Keywords: Sexual self-consept_Genital self-concept_sexual self-image_genital self-image_Sexual body-image

Introduction of different varieties of SARS COVID 2 (Review)

Hassan Zarghami far,[1,*] mehdi Zarghami far,[2] Hossein zarghami far,[3]

1. University of Zabol
2. Chabahar Maritime University
3. University of Zabol

Introduction: The emergence and rapid spread of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), a potentially fatal disease, is swiftly leading to public health crises worldwide. The origin of SARS-CoV-2 infection was first reported in people exposed to a seafood market in Wuhan City, China in December 2019. During the epidemic, the acute respiratory syndrome of coronavirus 2 (SARS-CoV-2), the cause of coronavirus disease, has different strains. Some types of SARS-CoV-2, which are in the category of variants of interest (VOI) and variants of concern (VOC). Since July 2021, four types of variants of concern (VOC) have emerged and ongoing genomic surveillance is essential for early detection of such variants Four types of variants of concern (VOC) : Alpha (B.1.1.7), beta (B.1.351), gamma (P.1) and delta. (B.1.617.2). Alpha (lineage B.1.1.7): It was first identified in October 2020 in the United Kingdom during the Covid-19 epidemic in the United Kingdom. The transmission rate of this virus is about 40 to 80% higher than the original virus. The virus has been observed in 12 countries until May 2021. Beta (lineage B.1.351): This variant was first observed on December 18, 2020 in South Africa. Unlike the original type of Covid 19, the virus has a high potential for infecting young and healthy people and is more dangerous. Also, several mutations in this virus increase the ability of the virus to attach to human lung cells and increase the ability to spread the virus. Gamma (lineage P.1): The gamma type was identified on January 6, 2021 by the Japan National Institute of Infectious Diseases (NIID) in Tokyo. The new species was first identified in four people who left the Brazilian state of Amazonas for Tokyo on January 2, 2021. On January 12, 2021, 13 local gamma-infected individuals were identified in the Amazon rainforest. This type of virus has 17 unique amino acid changes, 10 of which occur in its spike protein. Delta (lineage B.1.617.2): Delta was first discovered in India in October 2020 and has since spread internationally. Five types of variants of interest (VOI): Eta variant, also known as lineage B.1.525, is SARs-COV-2 virus strain that carries the same E484K-mutation as found in the Gamma, Zeta, and Beta variants. Unlike Alpha, Beta, Gamma, it does not carry the N501Y mutations. As per reports, this viral strain also carries the same deletion of amino acids histidine and valine in positions 69 and 70, found in Alpha, N439K variant (B.1.141 and B.1.258) and Y453F variant. Iota (B.1.526): Iota variant, It was first detected in New York City in November 2020. The variant has appeared with two notable mutations: the E484K spike mutation, which may help the virus evade antibodies, and the S477N

mutation, which may help the virus bind more tightly to human cells. Kappa (B.1.617.1): Kappa variant was first detected in India in December 2020,The Kappa variant has three notable alterations in the amino-acid sequences, all of which are in the virus's spike protein code. variant (C.1.2): cientists in South Africa have discovered a new viral variant of SARS-CoV-2,It's not a single virus but a clustering of genetically similar viruses, known as C.1.2. The researchers, in a pre-print study released , found this cluster has picked up a lot of mutations in a short period of time. SARS-CoV-2 Lambda is now expanding in some South American countries. However, its virological features and evolutionary features remain unknown. Lambda spike protein is more infectious and is attributed to T76I and L452Q mutations. This variety has seven unidentified mutations in the Spike gene (Δ247-253, G75V, T76I, L452Q, F490S, T859N) and deletion of the ORF1 gene Δ3675-3677, which neutralizes the antibodies and since the receptor binding domain (RBD) of the SARS protein -CoV-2 S has dominant immunity, mutations in this area can lead to immune escape. Both classes of variants are concerned with numerous mutations in their spike proteins and are relatively resistant to neutralizing antibodies (NAbs). In addition, mutations in the N-terminal domain (NTD) of the SARS-CoV-2 S protein are associated with volatile neutralization. Antibodies that increase viral infection (booster antibodies (EAbs)) have also been detected in severely ill patients, and these EAbs target the N-terminal domain of the NTD.

Methods: This article is a review and does not use laboratory or research methods

Results: This article is a review and does not use laboratory or research methods

Conclusion: SARS COVID- 2 has different variants, which are classified into two categories. 1-variants of concern (VOC) 2- variants of interest (VOI) Four types of variants of concern :Alpha ,beta, gamma and delta. Five types of variants of interest (VOI): Eta, Iota , Kappa , variant (C.1.2) and Lambda . SARS COVID 2 is constantly mutating, and the only way to fight the virus, in addition to following health protocols, is to vaccinate people at high speed around the world, and until the whole world is not vaccinated against the virus, the virus will always mutate. And displays more complex versions of itself. The main reason for the mutations in this virus is the lack of rapid vaccination of the people of the world, and until the vaccine is distributed evenly and fairly around the world, this problem will exist and we will see the spread of the mutations of this virus. The lambda spike protein has mutations L452Q and F490S in the RBD, and G75V, T76I mutations and 246-252 deletions in the N-terminal domain (NTD).

Keywords: SARS COVID-2 ; COVID -19 ; lineage ; variants ; mutation.

Investigating adverse effects and advantages of chimeric antigen receptor T (CAR-T) cell therapy for cancer patients : A Systematic Review and Meta-Analysis (Review)

Minoo Momenzadeh,[1] Mohammad Amin Talebpour,[2,*] Zahra Yaghubi,[3]

1. School of Medicine, Mashhad Islamic Azad University, Mashhad, Iran
2. School of Medicine, Mashhad Islamic Azad University, Mashhad, Iran
3. School of Medicine, Mashhad Islamic Azad University, Mashhad, Iran

Introduction: Cancer remains a devastating disease as existing therapies are too often ineffective and toxicities remain unacceptably high. Chimeric antigen receptor T (CAR-T) cells are engineered T cells which have been developed in recent years as a breakthrough in cancer therapy. CAR T cells are effective against both solid tumors and hematological cancers.It is important to evaluate the risk factors before starting this new anti-cancer therapy because physicians do not yet have sufficient clinical experience. Therefore the aim of this study is to investigate the adverse effects and advantages of chimeric antigen receptor T (CAR-T) cell therapy for cancer patients.

Methods: This review was performed within articles published at PubMed, Google scholar and Embase from 2015 to 2021. The keywords were Cancer, Chimeric antigen receptor T (CAR-T) cell,Treatment and Adverse effects. By searching this database,99 articles were found, 24 of them were not related with investigating and 52 of them by reading abstract were removed. All articles chosen from English articles.

Results: Finally 23 articles were included in the study. Some studies have discussed the benefits of CAR T-cell therapy and said that these therapies have improved the quality of life and survival of cancer patients. Some researches have shown that the success of this method in treating solid tumors has been limited. And there are also a number of adverse events, cardiotoxicity is one of the most harmful effects of anticancer therapeutics. The incidence of CAR T cell-associated cardiotoxicities was shown to be as high as 26% and thought to be primarily mediated by cytokine release syndrome. There are no standardized guidelines for the treatment of cytokine release syndrome or associated cardiotoxicity. After that, neurotoxicity is the most common noncardiac adverse event. Available evidence suggests that pretreatment evaluation, close monitoring, and early intervention may reduce these effects.

Conclusion: although multiple adverse events associated with CAR-Ts have been observed in small studies, but no large-scale studies exist. As a result, more large-scale research on the pathophysiology of disorders as well as new

approaches to overcome the challenges associated with this treatment is suggested.

Keywords: Cancer, Chimeric antigen receptor T (CAR-T) cell,Treatment,Adverse effects

Investigating anxiety like behavior and P2Y gene expression changes in the cerebral hemisphere of male rats during copper toxicity and treatment with vit C (Research Paper)

Somaye Asadipour,[1,*] Homeira Hatami,[2] Seyed Mehdi Banan,[3]

1. Department of Animal Biology, Faculty of Natural Sciences, University of Tabriz, Tabriz, Iran
2.
3. Department of Animal Biology, Faculty of Natural Sciences, University of Tabriz, Tabriz, Iran

Introduction: Divalent ions such as copper are essential for proper brain function but high levels of copper can be toxic by causing oxidative stress. To control this effects we can use vitamin c as an antioxidant. P2Y receptors are a family of purinergic G protein-coupled receptors, stimulated by nucleotides such as adenosine triphosphate, adenosine diphosphate. There is linkage between purinergic P2Y receptors and mitochondria toxicity. In this study we measured the P2Y gene expression changes and anxiety like behaviors in rats following copper toxicity and treatment with vit C.

Methods: Eighteen male Wistar rats were divided into three groups (n=6). Control, copper sulfate (10 mg/kg; i.p) and vitamin C (100 mg/kg; i.p) and copper sulfate +vitamin C (100 mg/kg; i.p) doses for 10 days. The exploratory behavior and general activity of animals were evaluated by elevated plus maze after injection. After receiving treatments, the animals were decapitated and their cerebral hemispheres were removed and the expression of P2Ygene assayed using RT- PCR. One-way ANOVA and post-hoc Tukey test were used for data analyzing.

Results: Data analyzing showed that the frequency of entry in the open arm of the elevated plus maze device in vitamin C receiving group and copper sulfate + vitamin C receiving group, decreased compared to the control group ($p<0.01$, $p<0.05$ respectively). The frequency of entry in the open arm in the group receiving copper has no significant difference compared to the control group ($p>0.05$). There is no significant difference between vitamin C group and copper sulfate + vitamin C group compared to the control group ($p>0.05$). There is no significant difference between vitamin C group and copper sulfate + vitamin C group ($p>0.05$). The duration of presence in the open arm of the elevated plus maze device in copper sulfate group and vitamin C group, significantly decreased compared to the control group ($p<0.001$). The duration of presence in the open arm in copper sulfate group and vitamin C group, significantly decreased compared to the copper sulfate + vitamin C group ($p<0.001$). There is no significant difference between copper sulfate + vitamin C group and control group ($p>0.05$). There is no significant difference

between vitamin C group and copper sulfate group ($p>0.05$). The P2Y gene expression in copper sulfate + vitamin C group, increased compared to the vitamin C group ($p<0.001$). There is no significant difference between copper sulfate group and vitamin C group and copper sulfate + vitamin C group compared to the control group ($p>0.05$). There is no significant difference between vitamin C group and copper sulfate + vitamin C group, compared to the copper sulfate group ($p>0.05$).

Conclusion: Surprisingly data analyzing showed administration of vitamin C alone and with copper increased the rate of anxiety like behaviors and most of animals did not experience of open arm entry. Also the usage of vit c with copper increased the level of p2Y gene expression. May be the co-administration of vit c and copper is needed to start p2Y gene expression but more research is necessary.

Keywords: Copper sulfate, Vit C, P2Y gene expression

Investigating coping strategies and psychological well-being of Sabzevar University of Medical Sciences Students during the Covid Pandemic 19 (Research Paper)

Zahra Zare ,[1,*] mina ghalenovi,[2]

1. Department of Midwifery, Faculty of Nursing and Midwifery, Sabzevar University of Medical Sciences, Sabzevar, Iran.
2. Department of Midwifery, Faculty of Nursing and Midwifery, Sabzevar University of Medical Sciences, Sabzevar, Iran.

Introduction: An increasing number of universities around the world have postponed or canceled their teaching activities due to growing concerns about the Covid 19 epidemic. Preventive measures following the Covid Crisis 19 endanger the mental health and psychosocial function of individuals. The aim of this study was to investigate t coping strategies and psychological well-being and students of Sabzevar University of Medical Sciences during the Covid 19 pandemic.

Methods: This descriptive-analytical study was performed on 126 students of Sabzevar University of Medical Sciences in 1399-1400 through available and online sampling. Data collection tools were demographic information questionnaire, Reef Psychological Well-Being Scale, and Blinges-Whames coping styles. Data analysis was performed using SPSS software (version 24), descriptive tests, independent t-test, analysis of variance, Pearson and linear regression.

Results: The mean score of psychological well-being of the students participating in the study was 78/5± 81/67 &4/79% had high psychological well-being.The mean score of problem-oriented coping strategies of the students participating in the study was 04/3± 55/15and emotion-oriented strategies were 91/5± 43/18.There was no significant relationship between the mean total score of coping strategies and psychological well-being (0/05<="" p="">

Conclusion: Due to the crisis caused by covid19 and its impact on mental health, it is suggested that administrators and educational planners, by holding workshops and counseling sessions for students, promote problem-based coping strategies in students.

Keywords: Psychological well-being, coping strategy, Covid19, student

Investigating of IL12B gene expression in blood cells of patients with Secondary Progressive MS in zanjan (Research Paper)

Katayoon Rahmani,[1] Sanaz Mahmazi,[2,*] Mohsen Kalantari,[3]

1. Department of Genetics, Zanjan Branch, Islamic Azad University, Zanjan, Iran.
2. Department of Genetics, Zanjan Branch, Islamic Azad University, Zanjan, Iran.
3. Assistant professor of Molecular Genetics, Department of Genetics, Zanjan Branch, Islamic Azad University, Zanjan, Iran.

Introduction: Multiple sclerosis (MS) is one of the most common neurological diseases in adolescents. MS is usually seen in people between the ages of 15-50. MS is about three times more common in women than in men, and the disease can occur at any stage of life. The symptoms of Secondary progressive MS always begin as RRMS, but the clinical symptoms change in such a way that the patient experiences steady severe symptoms without being associated with acute attacks. The risk of infection in this type of MS is 2.5%. The main purpose of this study was to evaluate the expression of the IL-12B gene in the blood cells of patients with MS compared to normal samples.

Methods: In this study, blood samples were collected from healthy individuals for the control group as well as venous blood samples from patients with MS from the neurology of Valiasr Hospital in Zanjan. Written consents were obtained from all individuals in both patients and the control group. Then RNA extraction and cDNA synthesis were performed and the expression changes of IL12B and Bact as the Housekeeping gene were evaluated by Real-Time PCR. Finally, the results of Real-Time PCR were analyzed by Rest 2002 Software and related diagrams were drawn by Excel

Results: IL-12 gene expression in patients with SPMS increased 7.3 times compared with the control group. This change in expression was statistically significant and Bact gene was the reference gene.

Conclusion: The results of relative analysis of IL-12 gene expression in patients with SPMS compared to the control group showed that gene expression in these patients increased 7.3 times compared to the normal group. This change in expression was statistically significant. Data analysis was performed for all samples separately and in comparison, to the control group, most of the samples were statistically significantly different ($P < 0.05$). IL-12 gene is one of the most important biomarkers in MS, and the results of our study confirmed the increase of this gene in SPMS.

Keywords: IL12B, Bact, Housekeeping, cDNA

Investigating the association between gastric ulcer and gastric cancer (Review)

Fateme Valipour Baboly,[1,*] zeinab sadat moosavifard,[2]

1. BSc in Nursing, Department of Nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.
2. Department of Nursing, Faculty of nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.

Introduction: Gastric cancer is one of the most common and deadly cancers of the gastrointestinal tract. This type of cancer is more common in some parts of the country as well as in some blood groups. Gastric or peptic ulcer: It is one of the major causes of gastric cancer. Helicobacter pylori is one of the most common causes of gastric ulcer. Of course, some medications also include the cause of this disease. According to available statistics, a large number of people in our country are suffering from this disease. The purpose of this study is to investigate and analyze the effective factors in causing gastric ulcer and its relationship with gastric cancer so that an effective step can be taken in the treatment and improvement of the health of our people.

Methods: This study was compiled as a review using data collection from library sources and databases of PubMed, SID, Google Scholar, Science Direct and with the keywords gastric ulcer, gastric cancer, Helicobacter pylori, pathogenic genes between 2009 and 1397. Has been.

Results: Gastric or peptic ulcer: It is more common in some parts of Iran, such as the northwest of the country. Considering the bacterial and pharmacological agent, almost everyone has this disease. The disease has a global epidemic and with its pathogenic genes includes inflammation until cancer of the gastric epithelial tissue, which this bacterium with its pathogenic strains and genes leads to this disease.

Conclusion: Gastric cancer is one of the most common cancers and is also a deadly cancer. In addition to chemical and pharmacological agents, microbes such as Helicobacter pylori are also important factors in causing it. This bacterium is the natural flora of the mouth. If they enter the stomach, it can cause stomach ulcers and eventually stomach cancer.

Keywords: Cancer, Helicobacter pylori, Pathogenic genes, Prevalence of Helicobacter pylori

Investigating the cause of Turner syndrome and ways to diagnose it (Review)

Fatemeh Kharatnejad,[1,*]

1. Azad university of Dezful

Introduction: Turner syndrome is a genetic disorder. This disease is the most common chromosomal disorder in humans. Turner syndrome has a great impact on the development of women. The most common feature of people with the disease is short stature, which is characterized by the age of 5 years. In many patients, normal ovarian function is lost. Initially, the ovaries develop normally. But egg cells usually die before puberty, and most ovarian tissue decays before birth. Most affected girls are immature if they do not receive hormone therapy, and many are unable to conceive. A very low percentage of affected women regain their ovarian function by middle age. Cause of this disorder: Typically, women have two identical sex chromosomes. These two chromosomes are called XX. Typically, men have one X chromosome and one Y chromosome. These two chromosomes are called XY. In Turner syndrome, cells lose all or part of the X chromosome. This disease is seen only in women. Some physical characteristics of people with Turner syndrome: About 30% of women with Turner syndrome have a draped neck, low back line on the back of the neck, puffiness or Swelling (lymphoma) of the hands and feet, skeletal abnormalities, or kidney problems. Some people are born with a heart problem that can be very dangerous. Most affected women have normal intelligence. Developmental delays, learning disabilities, and behavioral problems may also occur. These symptoms vary from patient to patient. Types of Turner syndrome: 1_Classic Turner syndrome in which the X chromosome is completely absent. 2_ Turner Mosaic Syndrome, abnormalities that occur only on the X chromosome in some cells of the body. What causes chromosomal changes in Turner syndrome? It can happen for two reasons: 1_ A monosome where the X chromosome may not be passed on to the baby girl due to abnormalities in the father's sperm or the mother's egg. Therefore, the child has only one single X chromosome and thus he will suffer from Turner syndrome. 2_ Mosaicism that during the process of cell division, some mutations and errors in fetal growth may occur. Thus, the body loses a copy of the X chromosome. A missing or altered X chromosome in a baby girl can cause complex health problems. Some of the health effects of this chromosomal error include short stature and ovarian failure. Ways to diagnose this syndrome: In medical genetics laboratories, Turner disorder can be detected by evaluating and analyzing chromosomes by various molecular methods. Diagnosis of this syndrome before fetal birth can be performed through techniques such as karyotype, QF-PCR and MLPA Is done. If ultrasound and trimester screening of a woman during pregnancy are positive, diagnosis before Birth is done with one of the techniques mentioned. This can

be done by analyzing the fluid around the fetus Did. Diagnosis of Turner syndrome after birth is usually made by determining the peripheral blood karyotype and chromosomal examination of the individual. The study of this syndrome can be done non-invasively on the mother's blood serum. Depending on the indications Relevant (dual serum markers + special ultrasound called NT) fetal health test or multi-test Advanced NIPT can be done.

Methods: by study and review articles

Results: Diagnosis of this syndrome before birth can be done by methods such as karyotype, QF-PCR, MLPA. It can also be detected after birth by determining the peripheral blood karyotype and chromosomal examination.

Conclusion: This disease affects one of the female sex chromosomes and is due to the lack of an X chromosome in girls, which causes them to be short and reach puberty and infertility later.

Keywords: Turner Syndrome, X Chromosome, Diagnosis, Turner Mosaic Syndrome, Classic Turner Syndrome

Investigating the Effect of Cytarabine chemotherapy drug on Expression Changes of LncRNA NKILA in Acute Lymphoblastic Leukemia (Research Paper)

Sahar Eskandari,[1] Golnaz Asaadi Tehrani,[2,*] Sina Mirza Ahmadi,[3]

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Introduction: Acute lymphoblastic leukemia is a type of blood cancer that develops in the bone marrow from young white blood cells called lymphocytes. It can affect both adults and children, but it is most commonly diagnosed in children. This study aimed to see how Cytarabine, a chemotherapy drug, affected LncRNA NKILA expression in an acute lymphoblastic leukemia cell line (E6.1 Jurkat).

Methods: we examined two doses of 1 and 5µM of Cytarabine chemotherapy drug in this study. At 24 hours after cell passage, the Jurkat E6.1 cell line was treated with prepared doses of Cytarabine. After RNA extraction and cDNA synthesis, the expression changes of LncRNA NKILA and GAPDH (the reference gene), were investigated by Real-Time PCR. Finally, the data were analyzed by Rest 2002 Software, and the diagrams were created by Excel.

Results: Our outcomes revealed that the expression changes of LncRNA NKILA compared to the housekeeping gene (GAPDH) were significantly increased after 24 hours of treatment with Cytarabine at 5µM. According to the findings, a concentration of 5µM at a time of 24 hours was the best dose and time. At 24 hours, the expressions of LncRNA NKILA at doses of 1 and 5 µM were 0/829 and 1/024 respectively. (P <0.001)

Conclusion: According to the results of the study, LncRNA NKILA expression changes after treatment with Cytarabine in concentrations of 5µM were effective in upregulation of LncRNA NKILA expression with a rate of 1/024. Generally, in 24 hours, Cytarabine had a positive effect on the LncRNA NKILA Tumor suppressor gene decrease mechanism, and this increase in expressions was statistically significant (p-value< 0.001).

Keywords: NKILA, Cytarabine, GAPDH, cDNA

Investigating the effect of nocodazol small molecule on CRIS-PITCH efficiency for targeted integration of transgene Cassette in CHO cell (Research Paper)

Behnaz rahmani,[1] Mohammad Hassan Kheirandish,[2] Fahime shamsi,[3] Samaneh Ghanbari Mehrandooei2,[4] Fateme davami,[5,*]

1. Medical Biotechnology Department, Semnan University of Medical Sciences, Semnan, Iran
2. Department of Medical Biotechnology, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran
3. Medical Biotechnology Department, Semnan University of Medical Sciences, Semnan, Iran
4. Biotechnology Research Center, Pasteur Institute of Iran, Tehran, Iran
5. Biotechnology Research Center, Pasteur Institute of Iran, Tehran, Iran

Introduction: CRISPR/Cas9 have been recently introduced as an alternative tool in CHO cell line development as a dominant expression host to integration of the transgene into the predetermined site of the genome via homologous recombination (HR) that promotes stable and high transgene expression. In this technology, donor plasmid harbors the transgene flanked by long homology arms that made vector designing complex and costly. Recently microhomology-mediated end joining (MMEJ)-based method termed Cris-Pitch (Precise Integration into Target Chromosome) have been used donor with in vivo linearized short homologous sequence (5–25 bp) to site specific integration. However this method still displays low targeted efficiency. To address this challenge, we combined Cris-Pitch system with nocodazole as a small molecule. We found that nocodazole-arrested mitotic cells use MMEJ to fix DSB damage. Indeed we further improved Cris-Pitch mediated knock-in efficiency using nocodazole to target the transgene to the transcriptionally active site of CHO-K1 cell line.

Methods: The CHO-K1 cells were cultured in DMEM/F12 medium supplemented with 10% fetal bovine serum and 10% CO2 at 37°C incubator. The puromycin sensitivity was also determined. The day before transfection, approximately 65×103 cells/mL were cultured in 24-well cell culture plates. Cells in each well were co-transfected with 500 ng of Donor plasmid and 500 ng of all-in-one plasmid mixed with 3 µL of Lipofectamine 3000 and 2 µL p3000, in 50 µL of DMEM/F12. 31 hours after transfection cell culture medium was changed and media containing 40 ng/ml of nocodazole was added to the cells. (Cells in control group just received fresh medium without small molecule). CHO-K1 cells were incubated with nocodazole for 15 h, after 15 hour medium was changed with fresh medium. Cell synchronization have been evaluated by Flow cytometry. 72 hours after transfection, the cells were seeded in a 6-well plate and were selected with 3 µg/mL of puromycin for

approximately 12 days to obtain antibiotic resistant cell pool. Cell pool with the desired genome changes have been confirmed with 5′/3′ junction PCR, limiting dilution was done into the 96-well plates at a density of 1 cell/well for the isolation of individual clones. About 10 days after seeding into 96 well, the single colonies in some wells had grown enough to transfer from 96 well to 24 well plates. Each recovered clone was examined by 5′/3′ junction PCR to evaluate the rate of knock-in efficiency.

Results: Two single guide RNA (sgRNA) candidates were designed, for promoting Cas9 cleavage in the s100A gene cluster in CHO-K1 cells. The cleavage efficiency of both sgRNA were analyzed and sgRNA2 was selected for Cris-PITCh mediated integration of the transgene cassette into the s100a gene cluster in the CHO-K1 cell genome. Nocodazole chemically interferes with the organization of microtubules and causes cell arrest in G2/M phase. In this study 31 hours after the concomitant delivery of Cas9/sgRNA and donor plasmid. Cells were treated with nocodazole for 15 hrs to accumulate cells in the G2/M phase and avoid the following replication cycle. We applied flow cytometry to analyses distinct populations of cells in the different cell cycle and indicated that nocodazole treatment, arrested about 85% of cells in G2/M phase. When nocodazole was removed, a stable cell pool was generated by puromycin selection of transfected cells. limited dilution was done and we obtained 72 recovered single clones in Nocodazole-treated group and 33 recovered single clones in control group (without nocodazole treatment), among which 72 clones of nocodazole group, 51 were 5’/3’ junction positive and among 33 clones in control group, 9 were 5’/3’ junction positive. These results show that targeted transgene knock-in was successfully achieved. Knock-in efficiency for nocodazole group was 64% and for control group was 27%.

Conclusion: In this study we have successfully accompanied Crispr/cas9-based MMEJ with a (nocodazole) small molecule for improvement of Cris-PITCh knock-in efficiency. Here, we observed a marked increase (about 2.37 fold) in MMEJ activity. According to the previous studies HR-mediated repair pathway was gradually shut down when cells exited S phase. This finding suggests that these cells don’t use HR pathway, but the MMEJ pathway remains available to fix DSB in this cells.

Keywords: Cris-PITCh; small molecule; CRISPR/Cas9 system; MMEJ repair pathway

Investigating the Effect of Thiosemicarbazones complexes Cu on Expression Changes of LncRNA PCAT1 in Acute lymphoblastic leukemia (Research Paper)

Neda Maleki,[1] Golnaz Asaadi Tehrani,[2,*] Sina Mirza Ahmadi,[3]

1. Msc of Molecular Genetic Department of Genetics, Zanjan Branch, Islamic Azad University, Zanjan, Iran
2.
3.

Introduction: Acute lymphoblastic leukemia (ALL) is a cancer of the lymphoid of blood cells marked by the proliferation of immature lymphocytes in large numbers. Thiosemicarbazones are noted for their biological activity and ability to function as ligands. The purpose of this research was to investigate the effect of thiosemicarbazones complexes with Cu on expression changes of LncRNA PCAT1 in the acute lymphoblastic leukemia Jurkat E6.1 cell line.

Methods: In this research, Appropriate doses of the thiosemicarbazones complexes Cu were prepared according to the IC50 of the drug that consists of 15 and 16 µM. The Jurkat E6.1 cell line was treated by Cu 72 hours after cell passage. The expression changes of LncRNA PCAT1 and GAPDH as the housekeeping gene were investigated using Real-Time PCR after RNA extraction and cDNA synthesis. Finally, Rest 2002 Software was used to analyze the data, and Excel was used to create diagrams.

Results: The Results of the research showed that after 72 hours of treatment with thiosemicarbazones complexes Cu at 15 and 16µM concentrations, the expression of LncRNA PCAT1 decreased significantly as compared to the control group. According to the findings, doses of 15 and 16µM of Cu over 72 hours are the optimal concentrations and time for this drug's effect. The expressions of LncRNA PCAT1 were 0/765 and 0/771 at the specified concentrations and times.

Conclusion: According to the findings of the study of expression changes in LncRNA PCAT1 after treatment with thiosemicarbazones complexes Cu, both concentrations of the drug were successful in decreasing LncRNA PCAT1 expression. Overall, thiosemicarbazones complexes Cu had a positive effect on the LncRNA PCAT1 oncogene reduction mechanism over 72hour, and this reduction in expressions was statistically meaningful (p-value 0.001). thiosemicarbazone complexes Cu has a high potential for cancer control and treatment, according to evidence.

Keywords: PCAT1, thiosemicarbazones complexes Cu, GAPDH

Investigating the immune responses to SARS-CoV-2 (Review)

Esmaeil Ghorbanalinezhad,[1,*] Shohreh Moradkhani,[2]

1. Faculty of Department of Microbiology, Islamic Azad University of Tonekabon branch, Tonekabon, Iran
2. Master student of Food Microbiology, Iran University of Medical Sciences, Tehran, Iran

Introduction: SARS-CoV-2 is a novel coronavirus belongs to family Coronaviridae. It is a single-stranded RNA virus within a capsid comprised of matrix protein. The severity of COVID-19 is mainly related to host factors, especially cellular immune responses in patients. The immune system responds to SARS-CoV-2 with a innate and a combined adaptive responses where the body makes specific antibodies and T-cells. SARS-CoV-2 has managed to rattle the host immune system. During the infection of SARS-CoV-2, ACE2 is the receptor present in the host cells and hence the B cell epitope site. The immune response in patients with fatal severe COVID-19 includes three stages: normal or hypofunction, hyperactivation, and anergy.

Methods: Laboratory tests that detect antibodies to SARS-CoV-2 including rapid immunodiagnostic tests. Antibodies produces in response to MERS and SARS cross react with SARS-CoV-2 antibodies. The betacoronavirus genome encodes the S protein as a major inducer of host immune responses and elicits an immune response. A condensed report on several patents that describe vaccines for generating immunity such as Attenuated virus vaccines, DNA-based vaccines, Protein-based vaccines, Virus-like Particle Vaccines, mRNA-based vaccines.

Results: COVID-19, through hACE2 receptor, transduces genomic material into the host and mediates pattern recognition receptors (PRRs), especially TLR-3, TLR-7 and TLR-8, which detect persistence of viral particles in the cytoplasm, thus mediating a series of immune mechanisms and proinflamatory cytokines to induce CD8+ and CD4+ T cells. SARS-CoV-2 antigen peptide pools-stimulated-IL-2 and -IFN-γresponse can distinguish COVID-19 convalescent individuals from healthy donors.IL-6 results in the onset of respiratory distress and failure. The S protein is a targetable using antibodies. Current evidence indicates that Th1 response is key to the successful control of SARS-CoV-2. The kinetics of immune responses during COVID-19, determined that type I interferon (IFN) could be administered to patients with severe COVID-19 in the hypofunctional stage, and intravenous immunoglobulin (IVIG) and glucocorticoid therapy, low molecular weight heparin (LMWH) anticoagulation therapy and anti-infective therapy with antibiotics could be administered in the immune hyperactivation stage. .

Conclusion: Reduction of circulating NK cells and T-cell subsets in the Bronch oalveolar lavage fluid of patients with pneu¬monia, IgM antibodies detectable 7-10 day after disease onset and serocoversion developed in most patients recovered and antibody specificity for the RBD domain of S protein is infrequent. Patients with COVID-19 mounted IgG and IgM responses to SARS-CoV-2 proteins, especially NP and S-RBD, and suggest that patients who are infected could maintain their IgG levels, at least for 2 weeks. The development of neutralizing antibody is associated with the activation of T cells and NK cells.

Keywords: Investigate, Immune responses, SARS-CoV-2

Investigating the Outbreak, Control, and Prevention Aspects of Coronavirus (COVID-19) (Review)

Arezoo Hassani,[1] Golnaz Asaadi Tehrani,[2,*] Sina Mirza Ahmadi,[3]

1. Msc of Molecular Genetic Department of Genetics, Zanjan Branch, Islamic Azad University, Zanjan, Iran
2. Assistant professor of Molecular Genetics, Department of Genetics, Zanjan Branch, Islamic Azad University, Zanjan, Iran.
3. Assistant professor of Molecular Genetics Department of Genetics, Zanjan Branch, Islamic Azad University, Zanjan, Iran.

Introduction: A new virus from the coronavirus family has been endangering human society and other animals since late 2019. Concerns regarding the new coronavirus, or Covid-19, are that the globe is facing a deadly coronavirus epidemic for the third time in less than two decades. The goal of this study was to learn more about the disease's prevalence, control, and prevention.

Methods: This is a review that was conducted by searching PubMed and Google Scholar for the terms COVID-19 and New Coronavirus 2019. To get background information, a free search on the Google search engine is employed.

Results: The Covid 19 virus is transmitted through respiratory droplets and direct contact with virus-containing mucus, according to the study. One of the causes of the uncontrollable and surprising prevalence of this infection is the high incubation period and the way of transition in these asymptomatic periods, or mild symptoms or before starting the disease. According to the studies, the symptoms of the virus are severe in people with chronic diseases such as diabetes, hypertension, cancer, cardiovascular disease, and chronic respiratory diseases, and also the severity of the virus infection increases with age and no definitive cure has been found for it. According to the recent publications, the virus will not be entirely controlled in the next years, and 40-70 % of the world's population will be infected. Covid-19 is probably to be a new seasonal infection, according to most epidemiologists.

Conclusion: The outcomes showed that the coronavirus epidemic can be prevented by considering the methods of prevention and management of factors affecting its transmission. It should be noted that the proposed ways to certain cures of this disease are still being researched and tested. Currently, the only way to control coronavirus 19 is to have good personal hygiene, increase immunity and avoid being in crowded places, social distance, and finally vaccination.

Keywords: Covid-19, coronavirus epidemic, immunity system

Investigating the quality of life of the elderly in Iran (Review)

Mohammad mahdi mohammadi,[1,*] zeinab sadat moosavifard,[2]

1. BSc in Nursing, Department of Nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.
2. Department of Nursing, faculty of nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.

Introduction: Quality of life is one of the measurable criteria for determining the health needs and conditions of the elderly. Measuring health-related quality of life is a way of assessing the health status of adults, and it can be used to identify factors associated with good health, maintaining good performance, and improving quality of life. Therefore, the researcher decided to conduct a study to evaluate the quality of life of the elderly.

Methods: After searching in Iranian journal of Nursing and Midwifery Research, PubMed and Google SID, Google, Magiran using Persian keywords quality of life, elderly, Iran, 1654 articles were selected and after including inclusion criteria: relevance of title Subject article, availability of full text, Persian written language and exclusion criteria: sample selection from non-elderly, rural elderly Finally, 21 articles were conducted between 2005 and 2017 by census in 1398 to be included in the study.

Results: In this study, the elderly from 11 cities in Iran were included in the study. The sample size was 6447 people. 4824 people were randomly selected and 1623 people were selected non-randomly. The mean age of participants was 78.93 78 4.85 13 13.85 - 66.10 years. Demographic characteristics of the participants: (64% - 91.41) male, (90.59% - 36) female, (89.7% - 9.2) married, (73% - 1.76) illiterate and (82.8% - 26) People also had at least one underlying disease. There was a significant relationship between education level, income, gender, marriage, current health status and age with quality of life (P <0.05). However, the three articles did not identify each of the variables of gender, marital status, and age as a related factor. The total score was quality of life for the elderly (22.80 - 1.49 86 86.86 - 21.41). Mean score of the dimensions of quality of life in the dimension of social function (18/22 - 32/18 ± 2 / 78- 40/18), physical function (59.07 - 23.52 23 23 / 68-69 / 17), mental health (42/94 - 8/9 67 9/67 - 47/21), general health (71/60 - 97/17 ± 7/61 - 92/16), vitality and vitality (18.62 ± 33 / 62-44 / 41), was physical pain (27.1 - 83.9 9 9.86 - 43.6).

Conclusion: The findings showed that quality of life in old age is a complex, objective and subjective concept. The quality of life of the Iranian elderly was estimated to be moderate in all dimensions except vitality and vitality. The

social and psychological dimension of Iranian elderly is better than their physical function. This may be due to the physical pain reported by the participants. Since the quality of life in this period is easily threatened due to old age, it is important to consider the underlying factors affecting the quality of life of the elderly. Therefore, it is recommended to plan to improve the quality of life in all dimensions, especially the physical dimension and physical pain in the elderly population of Iran.

Keywords: Quality of life, the elderly, Iran

Investigating the relation between the role of HPV and cervical cancer incidence (Review)

Nazanin ghasemi varaki,[1,*] Touraj Rahimi,[2]

1. cellular and molecular biology department science faculty
2. Agricultural biotechnology plant production andh- genetics dept.agriculture faculty.shahre Qods branch -Islamic Azad University-Tehran-Iran

Introduction: Cervical cancer is the fourth leading cause of cancer and one of the main causes of death in women all around the world. Approximately 70% of cervical cancers occur in developing countries. Cervical cancer screening programs in developing countries have greatly reduced the incidence of the disease. Cervical cancer is a type of cancer that originates from cervical cells. Several factors involved in the development of cervical cancer, but in 90% of cases, human papillomavirus is the cause. HPV consists of a family of small, double-stranded DNA viruses that infect the epithelium. The aim of this review study is to investigate the possible association between the role of HPV in the development of cervical cancer.

Methods: The present study is based on scientific reports on the association of HPV virus in the incidence of cervical cancer, which was analyzed by searching and summarizing the results in scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: The results of several studies have shown that most of the people infected by HPV virus, do not develop cancer cells. And a weak immune system is a risk factor for cervical cancer due to this virus. Evidence has shown that 90% of cervical cancers are associated with squamous cell carcinoma and 10% are associated with adenocarcinoma and other cases. The degree to which HPV virus can cause cancer depends on its types that infect cervical cells, causing epigenetic changes and developing precancerous cells. Studies have shown that two different types of HPV can infect the genital areas: low risk HPV types HPV6 and HPV11 are the cause of benign warts and usually improve. And high-risk HPV types 45,33,31,18,16 are associated with genital cancer. The results have shown that cervical cancers with HPV16 were more common (99%).

Conclusion: In conclusion, according to the World Health Organization and the high incidence of cervical and genital cancers caused by HPV, show the importance of prevention principles and effective vaccinates in certain ages to control and prevent human papillomavirus.

Keywords: Cervical cancer, HPV, Papillomavirus

Investigation effect of cytotoxicity of carbon quantum dots and targeted carbon quantum dots (Research Paper)

zahra Shadman,[1,*] Mohamad Mahani,[2] Faeze Khakbaz,[3] Mehdi Yousefian,[4]

1. Department of Chemistry, Faculty of Chemistry and Chemical Engineering, Graduate University of Advanced Technology, Kerman, Iran.
2. Department of Chemistry, Faculty of Chemistry and Chemical Engineering, Graduate University of Advanced Technology, Kerman, Iran.
3. Department of Chemistry, Shahid Bahonar University of Kerman, Kerman, Iran
4. Department of Chemistry, Faculty of Chemistry and Chemical Engineering, Graduate University of Advanced Technology, Kerman, Iran.

Introduction: Carbon quantum dots can be prepared from precursors such as: glucose [1, 2], graphite [3, 4], carbon nanotubes [5], citrate [6] and so on. Carbon quantum dots have unique properties such as good conductivity, high chemical stability, low toxicity, good biocompatibility, broadband light absorption, high emission photoluminescence and optical properties, easy synthesis and low cost on a large scale [7]. The dimensions of the carbon quantum dots synthesized by hydrothermal method are 1.5-4.5 nm, which are used in bioimaging due to their low toxicity and ability to due to their photostability light. In 2018, Kong et al. Synthesized carbon dots by hydrothermal method using citric acid and ethylene diamine and examined its effect on MCF_7 and L_929 cancer cells in breast cancer. The synthesized carbon dots had a large capacity to load doxorubicin and also had a better antitumor effect in MCF_7 cancer cells [7].

Methods: In this study, carbon quantum dots were synthesized by hydrothermal method. First, citric acid and urea dissolved in distilled water and transferred to an autoclave, then incubated for 4 hours at 160 ° C in the oven. To prepare the modified carbon quantum dots, folic acid dissolved in phosphate buffer, then 200 µl of EDC solution and 200 µl of NHS solution was added to it, and after stirring for 30 minutes, and was added to it 1 ml of dilute solution of carbon quantum dots; and stirred for 24 h. Finally the carbon quantum dots-folic acid was obtained. Similarly, carbon quantum dots-hyaluronic acid and carbon quantum dots-mannose were synthesized.

Results: The particle size of the synthesized carbon quantum dots was 2 nm. Dilute solutions were prepared from carbon quantum dots, carbon quantum dots-folic acid, carbon quantum dots-hyaluronic acid and carbon quantum dots-mannose, and their absorption spectra were recorded; In the absorption spectra of carbon quantum dots and targeted carbon quantum dots, two peaks related to π - π * transitions and n-π * transitions were observed at 240 and 345 nm, respectively. Excitation spectra of carbon quantum dots at the

emission wavelength of 440 nm, which shows that the maximum emission intensity at the excitation wavelength is 345 nm. Binding of doxorubicin to carbon quantum dots and targeted carbon quantum dots was performed with a molar ratio of 4:1, and the highest binding between drug and targeted carbon quantum dots with hyaluronic acid was 50%. Drug release was investigated in a neutral and acidic environment, and most drug release (80%) was performed from targeted carbon quantum dots-hyaluronic acid in acidic environment. Cytotoxicity of carbon quantum dots was investigated by MTT assay. carbon quantum dots and targeted carbon quantum dots are non-toxic at all concentrations and do not cause cell death alone. Doxorubicin-bound carbon quantum dots also resulted in higher cell death at high concentrations, and 38.46% of cancer cells survived at the highest concentrations. At the highest concentrations of target quantum dots with folic acid, target quantum dots with hyaluronic acid and target quantum dots with mannose that bind to doxorubicin, 44.42%, 42.3% and 35.25% of cancer cells survived, respectively.

Conclusion: Targeting carbon quantum dots causes specific binding to receptors on the surface of cancer cells. Carbon quantum dots and targeted carbon quantum dots alone are non-toxic, but if the drug binds to them, they can cause death to cancer cell.

Keywords: Carbon quantum dots; Bioconjugation; Cellular toxicity.

Investigation of Changes in The Expression of Proinflammatory Cytokines Caused by Extract Silybum marianum L. in in-vitro and in-vivo (Research Paper)

Amir Akbarnejad Eshkalak,[1,*]

1. Payame Noor University . Tehran , Iran

Introduction: 1. Introduction: OA is a persistent, progressive infectious joint illness, that causes cartilage, and bone destruction. In addition to progressive destruction of articular cartilage, the disease develops with symptoms such as calcium crystal deposition (calcification) on cartilage, subchondral bone thickening, osteophyte formation, synovial inflammation, and chondrocyte hypertrophic differentiation of chondrocytes (1,2). However, the most frequent symptom and reason of disability is the pain in patients with osteoarthritis. Inflammation can accelerate the process of cartilage and bone destruction. One of the factors that cause inflammation is cartilage fragmentation and their floating in the synovial fluid that stimulates the synovial membrane and eventually causes synovitis. This inflamed membrane subsequently releases other inflammatory mediators that further damage the cartilage (3). We know that cytokines, along with growth factors, play a key role in the pathophysiology of osteoarthritis. They are intimately related to functional changes in the synovium as well as cartilage, followed by subcutaneous bone. Cytokines, along with growth factors, are secreted mainly by synovial membrane cells and propagated through cartilage by synovial fluid. In the process, they inactivate cartilage, resulting in the secretion of secondary metabolites such as pro-inflammatory cytokines as well as proteases. The major cytokines (anti-inflammatory) and antagonists - involved in the pathophysiology of OA such as the Interleukin 1 family, especially iL-1 α, iL-1β as well as interleukins include iL-4, iL-6, iL-8, iL-10, iL-11, iL-13, iL-17 besides TNF-α and iL-1Ra. Growth factors such as TGF-β, FGF, PDGF, and IGF are involved in OA, in which TGF-β has both a synthetic and a catabolic effect that depends on several factors such as concentration, target cell, and related tissue. (4,5). It is right that pro-inflammatory cytokines, especially iL-1β and TNF-α, play a major function in the onset and progression of the OA so that iL-1β causes cartilage destruction and TNF-α promoting the inflammatory process (6,7). Cartilage and synovial cells are stimulated by iL-1 beta and TNF-alpha, and produce other cytokines such as LIF, il-6 and iL-8, as well as prostaglandin E2 or PGE2 (8). The cytokine iL-1β plays a potential role in OA. It can independently induce catabolic effects and inflammatory response and combine with other intermediaries. It is one of 11 members of the IL-1 (IL-1F) family (9). In patients with osteoarthritis, it is observed that the concentration of IL-1β in the joint fluid and synovial membrane, as well as cartilage, is significantly increased (10,11). In the course of OA, Tumor necrosis factor-alpha (TNF-α), together with IL-1β have been identified as two very important

and fundamental factors occurring in the pathophysiological processes (12). TNF-α is made and splashed by the similar joint cells produced IL-1β, and an increase in its concentration is also noticed in the similar parts, like SF, SM, cartilage, and SCB layer, where rose amounts of IL-1β are also noted (13, 14). Besides the FLS cells, tumor necrosis factor receptors 1 are rose (15). Interleukin-6 is a complex distinguished by comprehensive interactions in actions taking place in human beings. It may be classified as anti-inflammatory interaction which powerfully operates the immune system and raises the inflammatory responses, even if several are considered of its results (16). IL-6 production in damaged joint tissues is normally in reaction to Interleukin -1β, TNF-α also is mostly mediated by osteoblasts, chondrocytes, adipocytes, FLS, and macrophages (17). An increase in the concentration of interleukin-6 in serum and synovial fluid has been observed and this increase is emphatically associated with the severity of wounds on X-ray body scans (18, 19, and 20). The effect that Interleukin -6 has on articular cartilage is no different from other cytokines, but it reduces the production of type 2 collagen and MMP enzymes. (21, 22). Interleukin-6 is known as the crucial cytokine, brings about variations in the subchondral bone layer (23, 24). It is influenced by osteoclast structure or bone defect while manifesting its cooperation with Interleukin -1β, and TNF (25). Another corporator of IL-18 is the Interleukin -1F family (26). At first, pro-interleukin-18 is like precursor form which has 192 amino acids but after activation of caspase-1 or proteinase-3, it reduces to 157 amino acids and switches to active forms. The rise of caspase-1 and articular cartilage or synovium cause to an active form of IL-18 and IL-1β (16). The creation of interleukin-18 is produced in osteoblasts, chondrocytes, macrophage, and FLS (27). There is a significant relationship between increasing gene expression of iL-18 in synovium, synovial fluid, blood serum, and cartilage and the severity of the disease seen in radiographic images (28, 29). One of the most widely used dietary supplements containing medicinal plants is the extract of milk thistle. This supplement is one of the most popular products in the United States (30). Silybum marianum L, also known as wild artichoke is a kind of herbal plant. Silymarin is an active ingredient in milk thistle (47). Silymarin is a combination of flavonoliganes containing silibinin A, silibinin B, isosilibinin A, isosilibinin B, silydianin, silychristin, isosilychristin as well as taxifolin flavonoid (37,70). silymarin consists of approximately 50 to 60% of Silibinin, 20% of Silicristin, 10% of Silydianin and 5% of Isosilybin and silibinin has the highest biological activity. (31,32). Milk thistle is discovered throughout the milk thistle, nevertheless is more focused on its seeds and fruits. The seeds of milk thistle hold a relatively high level of oil, about 18-31 percent rich in unsaturated fatty acids, of which 42-54 percent is linoleic acid and 21-36 percent is oleic acid (43). Silymarin is a compound contains various properties like anty-inflammatory hepatoprotective, antioxidant (33,34), heart-protective (36,37), hypocholesterolemic (37), anti-diabetic (38,39), anticancer (40,41), and cardioprotective activities. Clinical studies have been demonstrated that silymarin has very rare side effects at high doses (>1500

mg/day), however it has quick metabolism and penurious absorption (42). Although various treatment options are used to manage OA, these options do not affect on preventing the process of their degradation. Regularly used pharmacological agents include corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), and hyaluronan. Especially NSAIDs which are widely used and their long-term use is associated with serious side effects such as gastrointestinal lesions (48). The use of effective therapies with fewer side effects has led patients with OA to think of a way to control pain and confirm their function and quality of life. (43). The intention of these experiments is to treat OA and acquiring a path to block the process of articular cartilage destruction we strived to demonstrate a new method of treatment based on herbal medicine to cure and diminish the symptoms of disease and pain by using the AESM (Alcoholic Extract Silybum marianum L), furthermore to protect patients from the severe side effects of common chemical drugs. In this study, we used dexamethasone and ibuprofen as steroids and non-steroidal anti-inflammatory drugs (NSAIDs), respectively. Meanwhile, the rabbits became infected using monosodium iodoacetate (MIA) (44).

Methods: TAK (TAK-242) or the TLR4 signaling pathway suppressor as well as anti-TLR4 production of Sigma- Aldrich (St. Louis, MO, USA), alkaline phosphates conjugate, Secondary antibody consist of Goat Anti-Rabbit IgG (H+L) (Sigma-Aldrich, Germany), MTT or 3-(4,5- dimethylthiazol-2-y1)-2,5-diphenyltetrazolium bromide, CD90, CD68, CD14, and Vimentin, dimethylsulfoxide (DMSO) (Sigma-Aldrich, MO, USA). hematoxylin and eosin staining (H&E) (Bio-Optica, Italy). Bovine serum albumin (BSA), Fetal bovine serum (FBS), Dulbecco's modified Eagle's medium (DMEM)/Ham's F12 medium, and 0.25% trypsin ethylenediaminetetraacetic acid (trypsin–EDTA). (Gibco, Life Technologies Corp, USA). TRIzol reagent (Carlsbad, Calif., USA). In addition (MIA, 4mg/50µl, Sigma-Aldrich, MO, USA) and RNA isolation kit (Cinna Pure RNA Kit Cat. No.: PR891620, IRAN Tehran). Preparation of Silybum marianum L. Extract (ESM) Silybum marianum L was obtained from Iran's center of genetic resources. Then the plant was extracted under sterile conditions with a rotary evaporator vacuum device (Model 750, manufactured in West Germany). The ESM powder (1mg) needs to be soluble in DMSO and congested as aliquots (20 mM) at -20oC before reuse. Ethics In this research, the ethical ideology has been observed and acted by. We comply with international law on working with laboratory organisms. This paper was accepted by the Ethics Committee of the University of Payme Noor Tehran/Iran (IR.PNU.REC.1399.114). Animals and Husbandry Thirty healthy male New Zealand White rabbit sage 5 months, the average weight of 2.5 kg was used to investigate the role of AESM in osteoarthritis induced by MIA. The rabbits were maintained in an environment with precise temperature (25°C ± 1°C) and humidity settings(55% ± 15%), air conditioning, and regular light and dark cycles. All rabbits were retained in metal cages measuring

(35×50×25 cm) and allowed to access standard food (Industrial Expansion Development Co Behparvar, Iran) and ad libitum water. at any time of the day or night.

Results: 3. Results 3.1. Effects of Treatment on Body Weight At 35 days after surgery, the average weight of rabbits in each group was 2.39 ± 0.15, respectively. No significant difference in body weight was observed between the groups. 3.2. Effects of Treatment on Knee Thickness We accurately measured the diameter of rabbit joints before OA and then one week after OA and also after treatment. The mean joint diameter of rabbits was measured before the onset of the disease at 15.8 mm and this value increased to an average of 19.8 mm after MIA. Finally, after treatment, the rabbit joint diameter, although generally reduced, did not reach the initial mean and the average was recorded at 16.6 mm (Table 7). 3.3. Cytotoxicity assays Although cell cultures were served 24 hour with AESM, it did not bring about any changes in cell numbers at the concentrations of (1x10-3, 9x10-3, 1x10-2, 9x10-2, 1x10-1, 9x10-1, 1, 9,18, 36, 45, 54, 63, 72, 81, 90 and 100µg/ml). There is no sign of side effects higher than 1x-10 µg/ml. Enhancement of concentration 9 µg/ml leads to a particular diminished in the cell viability (LC50 was calculated 45µg/ml and its average was 12.38 µg/ml) (56)(Fig.6). 3.4. The result of AESM in RFLS RFLS cells natured for 3 days in the medium lonely, AESM leads to decrease the level of genes such as iL-1, iL-6, iL-18, and TNF-α regarding to LPS-induced chondrocytes (Table 4 and Fig.3). Operated of cells by 20 ng/mL of LPS caused a remarkable rise in the articulation of the proinflammatory cytokines. As expected, dexamethasone and NSAID had a significant effect on reducing the expression of cytokines in stimulated cells, but DMSO did not affect. The AESM almost caused a decrease in the percentage of cells stimulated by 50% which is a significant decrease compared to Dexamethasone and NSAID (Table 4,6 and Fig. 3). 3.5. The Effect of AESM on Cytokine Gene Expression in Cartilages The plant extract was able to compete with chemical drugs and also had a significant effect on reducing inflammation and decreasing the process of joint cartilage destruction. The highest impact effect of AESM after the iL-1 at 29.85 is related to iL-18 at 49.48(Table 5 and Fig.4). Similar results were obtained in the articulation of the Interleukin-6 and Tumor Necrosis Factor-α genes which was acceptable. 3.6. The Change in serum level of proinflammatory cytokines Examination of blood samples and analysis of its data indicated that consumption of AESM not only significantly reduced the expression of pro-inflammatory genes in the blood, especially iL-6 but also proved its anti-inflammatory properties and confirmed the results of former tests. Therefore, it can be a worthy therapeutic purpose for OA patients in the future. We believe that the effects of the AESM on reducing pro-inflammatory genes expression will be more severe with increasing concentration (Fig.5). 3.7. Rabbits histological evaluation Thickening of the middle part of cartilage in rabbits was done by hematoxylin and eosin staining (H&E) (Bio-Optica, Italy) and the

results are shown on Figure 7. The concentration of proteoglycans and elastin fibers in the matrix of cartilage in the group of rabbits with OA treated with AESM was obviously increased compared to the control group($P<0.05$). According to the results, it can be mentioned that the plant extract has increased the thickness of the middle part of cartilage in rabbits with OA. Due to the high amount of essential fatty acids, AESM has caused the accumulation of indispensable proteoglycans of cartilage. Increasing cartilage thickness and accelerating the healing process of cartilage wounds and accumulation of proteoglycans in the group treated with AESM indicate that AESM has been able to improve articular cartilage and help treat OA (Fig 7).

Conclusion: 4. Discussion OA is known as a joint illness distinguished by inflammation of the synovial membrane and progressive loss of extracellular matrix proteins and gradual destruction of articular cartilage and is the best source of physical disease (58,59). The biochemical cause of OA is still unknown, but the onset of the disease usually begins with the formation of abnormal structures in the joint or abnormal pressure on the joint surface (60). Nowadays, no satisfactory and definitive treatment has been developed for OA (61). Common treatments for OA include pharmacotherapy, non-pharmacotherapy, supplementation, and surgery (62). Non-specific cyclooxygenase inhibitors (COX-II) Non-steroidal anti-inflammatory drugs (NSAIDs) and oral analgesics such as acetaminophen (63), antidepressants, and glucosamine are used in combination with intra-articular injections of steroids and hyaluronic acid derivatives (64,65). Unfortunately, the use of these chemical drugs has many side effects such as severe gastrointestinal bleeding and digestive disorders, and has severely limited the use of this treatment by patients (66). Therefore, in this study, we are in pursuit of an appropriate therapeutic method to reduce the symptoms of the disease and pain with the least side effects in patients. Our method is a complementary, and alternative treatment method. We used the medicinal plant Silybum marianum L,(AESM) to treat sick rabbits and evaluated the effect of injecting administration of AESM in comparison with NSAIDs and steroid drugs in vitro or in vivo. Accurate identification of the components of AESM is possible using HPLC-UV (67,68). Milk thistle seeds contain 4 to 6% silymarin and its extract contains 65 to 80% silymarin (69) and about 25 to 35% of the oil full of fatty acids. The highest concentration of fatty acids is 48.88% unsaturated fatty acid Linoleic acid (70). The compounds are divided into two main groups, flavonolignans and non-flavonolignans, and Non- flavonolignans group itself is divided into two smaller groups, polyphenolic compounds, and flavonoids. Finally, the flavonoids group can be divided into taxifolin and quercetin. Silibinin (or Silybin) has the highest concentration and maximum biological properties among other components of silymarin (69-71). In OA, immune cells potentiate the inflammatory process in the joint by secreting proinflammatory cytokines such as Interleukin -6, Interleukin1-α, Tumor Necrosis Factor-α and Interleukin -1β (72). Interleukin -1β is not expressed by tissues under normal

and physiological conditions of the body (73) and is first synthesized as pro-iL-1β, which is biologically inactive and converted to active iL-1β after caspase-1-dependent proteolysis (74,75). In addition, interleukin-1β is activated by neutrophils-derived elastase and cathepsin-G and mast cell-derived proteolysis (76,77). Unlike iL-1β, iL-1α does not require primary processing for biological activity and activation. Activated iL-1β along with iL-1α both persuade many cytokines and play an important role in the body's irritant response (78,79). Interleukin -6 is known as a proinflammatory cytokine required in many incurable inflammatory illnesses secreted by joint tissue and, after binding to its soluble receptor (iL-6R), transsignals and activates the immune system by calling mononuclear cells (such as monocytes) to the inflamed area of the joint (80). TLR4 activates the MyD88 pathway in the plasma mambrane. Then it enters the cytoplasm through CD14 dependent endocytosis and initiates the TRIF-dependent cascade. Also, TRIF activates TRAF3, TRIF3 which causes the release of type 1 interferons and CCL5. TRAF6 activates three important signaling pathways after TAK1 including AP-1, CREB and NF-κB. They increase the expression of proinflammatory cytokine genes such as iL-6, TNF-α , pro-iL-1β and pro-iL18. Our researches revealed that AESM has an ability to suppress the TLR4 signaling pathway and also the reduction of genes expression such as iL-1α, iL-6, iL-18 and TNF-α on plasma and after the induction of RFLS cells induced by MIA and AESM. Staining of cartilage cells by H&E method showed that AESM can also inhibiting inflammation accelerates of the healing process of articular cartilage (81). 5. Conclusion: As we know, during OA disease, the immune system is activated by increasing the expression of proinflammatory cytokine genes such as iL-1α, iL-18, TNF-α, and iL-6 by immune cells and cartilage cells at the joint surface, the destruction of articular cartilage begins, intensifies progressively and eventually leading to cell death. Today, the drugs used to treat OA are not very effective and also have dangerous side effects. Therefore, patients are less inclined to take these drugs. This study aimed to find and propose a drug to reduce the symptoms of OA and treat it with minimal side effects and increase the community's hope for definitive treatment of osteoarthritis. In this paper, we examined the ESM effectiveness, on rabbits with OA. The rabbits became ill by injecting MIA into the wrist joint. After 60 days of treatment of rabbits with AESM, we measured the gene expression of proinflammatory cytokines including TNF-α, iL-6, iL-1α and iL-18. Also, we compared the effect of AESM with Dexamethasone and Ibuprofen(NSAID), on the expression of those genes related before. Our experiments indicated that consumption administration of AESM reduces the expression of TNF-α, iL-6, iL-1α and iL-18 genes and can compete well with common drugs in the treatment of OA. Reduction of expression of these cytokines in articular cartilage cells as well as immune cells (such as monocytes and macrophages) cause reduce joint inflammation and symptoms such as pain, swelling, and inflammation gradually disappear. We suggest that with further research on the medicinal plant milk thistle and its seeds

extract, this plant can be introduced as a very effective and efficient drug to reduce joint inflammation, pain, and decrease the expression of proinflammatory cytokine genes and a new treatment for OA with minimal side effects.

Keywords: Silybum marianum L, monosodium iodoacetate, pro-inflammatory cytokines, osteoarthritis

Investigation of Frequency of Human Papillomavirus Infection and it's genotypes among Patients with Colorectal Cancer in Bushehr Province, 2009-2018 (Research Paper)

Fatemeh Farshadpour,[1] Reza Taherkhani,[2,*]

1. Department of Virology, School of Medicine, Bushehr University of Medical Sciences
2.

Introduction: Background and aims: Colorectal cancer is one of the most important malignant tumor in humans and the third most common cancer in men (after lung and prostate cancer) and the second most common cancer in women (after breast cancer) worldwide. The role of infectious agents and oncoviruses such as human papillomaviruses in contaminating colorectal regions, which can occur as a result of dissemination from contaminated anogenital areas or through blood or lymph, is mentioned as a potential risk factor for colorectal cancer. This study was conducted to determine the prevalence and genotype distribution of human papillomavirus in paraffin-embedded tissue specimens from patients with colorectal cancer in a 9-year period in Bushehr province using nested-PCR technique.

Methods: Materials and Methods: This study is a descriptive cross-sectional study. The study population includes paraffin-embedded colorectal specimens of patients with colorectal cancer referred to the Shohadaie Khalij-Fars Hospital in Bushehr during 2009 to 2018. Of 147 patients, paraffin-embedded tissue specimens from 128 patients with colorectal cancer were investigated for molecular analysis. In addition, 146 non-cancerous paraffin-embedded tissue samples (inflammatory and polyp specimens) were used as control group. Data were analyzed using SPSS software, Chi-square and Fisher's statistical tests.

Results: Results: Out of 128 patients with colorectal cancer, 65 men with a mean age of 59.05 ± 13.05 and 63 women with a mean age of 56.79 ± 15.86 were enrolled. Most of the patients were between the ages of 50- 59 years. Most cases of colorectal cancer were from 2014 and 2015. The overall prevalence of HPV infection in 128 colorectal cancers was 1.56%. Out of 98 samples with colon adenocarcinoma, the prevalence of HPV infection was 1.02% and among 30 cases with adenocarcinoma rectum, the prevalence of HPV infection was 3.33%. Although the prevalence of HPV infection in adenocarcinoma rectum biopsy specimens was higher, the results indicated no significant statistically association between the anatomical location of the tumor and the prevalence of HPV infection. In addition, 146 non-cancerous colorectal specimens including 104 inflammatory and 42 polyp specimens were negative for HPV infection.

Conclusion: Conclusion: The overall prevalence of HPV infection in colorectal cancer samples was low, and there was no significant statistically relationship between age, sex, city, year and anatomical location of cancer with the prevalence of HPV infection (p value> 0.05). Therefore, the role of other risk factors for colorectal cancer such as unhealthy diet, obesity, smoking, genetic factors and environmental factors may be more important than the role of human papillomavirus in the development of colorectal cancer.

Keywords: Human Papillomavirus, Colorectal Cancer, Bushehr province, nested-PCR method

Investigation of Frequency of Human Papillomavirus Infection and it's genotypes among Patients with Lung Cancer in Bushehr Province, 2011-2018 (Research Paper)

Reza Taherkhani,[1] Fatemeh Farshadpour,[2,*]

1. Department of Virology, School of Medicine, Bushehr University of Medical Sciences
2. Department of Virology, School of Medicine, Bushehr University of Medical Sciences

Introduction: Lung cancer is very important in terms of the incidence and mortality rate of cancer around the world and is more prevalent among men than women. The disease is usually diagnosed in advanced stages, which reduces the survival rate. The role of oncoviruses such as human papillomaviruses in contaminating lung, which can occur as a result of diffusion through airways or through blood or lymph, is mentioned as a potential risk factor for lung cancer. This study was conducted to determine the prevalence and genotype distribution of human papillomavirus in paraffin-embedded tissue specimens from patients with lung cancer in an 8-year period in Bushehr province using nested-PCR technique.

Methods: This study is a descriptive cross-sectional study. The study population includes paraffin-embedded lung specimens of patients with lung cancer and non-cancerous lung tissue biopsy referred to the Shohadaie Khalij-Fars Hospital in Bushehr during 2010 to 2018. Of 75 patients with lung cancer, cancerous paraffin-embedded tissue specimens from 63 patients and 56 non-cancerous paraffin-embedded tissue samples (Inflammatory tissue, fibrotic, granulomatous, neodular and hemorrhagic specimens) as control group were investigated for nested PCR method. Data were analyzed using SPSS software, Chi-square and Fisher's statistical tests.

Results: The mean age of 75 patients with lung cancer was 68.05 ± 13.58 years with age range from 31 to 93 years. Most of the patients with lung cancer were between the ages of 60-79 years. Most cases of lung cancer in Bushehr city were from 2015 and 2016. The most common type of lung cancer was squamous cell carcinoma (60%). The overall prevalence of HPV infection was negative in 63 cases of lung cancer. In the control group, among 56 non-cancerous lung tissue samples, HPV infection was observed in only one case of 74-year-old female sclerotic lesion, and the overall prevalence of HPV in the control group was 1.8%.

Conclusion: The overall prevalence of HPV infection was negative in lung carcinoma specimens, and in the control group (non-cancerous), only one

case of HPV (low risk) was positive. In addition, there was no significant statistically relationship between age, sex, city, year and type of cancer and non-cancerous lung lesions with the prevalence of HPV infection (p value> 0.05). Therefore, the role of other risk factors for lung cancer such as age, smoking, diet, genetic factors and environmental factors may be more important than the role of human papillomavirus in the development of lung cancer.

Keywords: Human papillomaviruses, Lung carcinoma, Bushehr province, Nested-PCR

Investigation of Long Non-coding RNA HOX A11-AS Expression in Iranian Patients with Glioblastoma (Research Paper)

mansoureh shabani,[1,*]

1. Islamic Azad University, Science and Research Branch, Faculty of Basic Sciences, Department of Genetics

Introduction: Glioblastoma is one of the most malignant and common brain tumors, accounting for about half of all gliomas. Glioblastoma is a central nervous system tumor that originates from the glial tissue of the brain. The present study aimed to investigate changes in the expression of long non-coding RNA HOXA11-AS as a possible biomarker in glioma

Methods: For the purposes of the present study, first, the medical records of the patients in Imam Hossein Hospital in Tehran, Iran were reviewed. The ethical considerations were respected as well; accordingly, written informed consent was obtained from the patients and the code of ethics was achieved as well. Finally, the paraffin blocks, including the biopsy of brain tumor tissue of the patients who referred to Imam Hossein Hospital during 2015-17 were collected and their degrees were confirmed by the pathologist. In total, 50 samples of grades 1 and 2 as well as 50 samples of grades 3 and 4 were examined in this research project. The RNA extraction and cDNA synthesis were performed for all the tissue samples donated by the patients. Subsequently, a specific primer and probe were designed and the expression of the HOXA11-AS gene was investigated using real-time polymerase chain reaction technique. The mean age of the subjects was 43.70±16.416 years. The collected data were analyzed in SPSS software (version 20) using descriptive and analytical statistics. Moreover, the expression levels of this gene in lower- and higher-grade tumor tissues were compared using the unpaired samples t-test.

Results: Based on the results, the tumor samples with grade three and four underwent a 2.76 fold increase in expression (fold change), compared to tumor samples with grade one and two. This difference was statistically significant.

Conclusion: Based on the findings, it can be concluded that the expression of the HOXA11-AS gene has a significant positive relationship with the degree of disease (P=0.0002).

Keywords: Glioblastoma; HOXA11 protein; Long non-coding RNA

Investigation of the effect of bicarbonate (HCO3-) signals on sperm flagellum movement in humans (Review)

Ali Ahmadi,[1,*]

1. Student, Faculty of Biological Sciences and Technologies, Islamic Azad University, Sari, Iran

Introduction: Mammalian flagellum is a special type of motor fluid that is required for sperm motility and male fertility. The effective movement of the flagellum depends on axonal function, which in turn depends on the appropriate ion homeostasis in the flagellum chamber. All of these physiological processes are also possible due to the micro-orchestrated signaling pathways between skeletal protein complexes and plasma membrane elements, such as ion channels and carriers. The aim of this study was to investigate the effect of bicarbonate (HCO3-) signals on sperm flagella in humans.

Methods: This study was conducted in 2021 by searching for keywords such as bicarbonate signal, sperm flagellum and sperm motility in valid databases such as: pub med and google scholar, which finally found 15 articles, of which 15 articles 10 articles were used

Results: Based on studies from articles, the results show that HCO3- is a key factor in regulating sperm motility. High concentrations of HCO3- in the female reproductive system increase the frequency of sperm, which promotes sperm through the female reproductive system. Carbonic anhydrides (CA), which catalyze the reversible hydration of CO2 to HCO3-, are potential candidates for regulating HCO3- homeostasis in sperm and the composition of the male and female reproductive fluids. Provides a high concentration of bicarbonate High concentrations of bicarbonate are very important for the capacitor. In particular, HCO3- is present directly in bicarbonate-dependent solution, which activates bicarbonate-dependent solution cyclase. Quotes work to provide a stable setting of Cl− transitions. In the epididymis, including the cap, body, and caoid epididymis, low bicarbonate concentrations and acidic pH of the lumen are important for maturation, storage, and fertility of sperm. , Which makes significant changes along the epididymal duct. Several channels and ion transport, such as cystic fibrosis transmission conduction regulator, bicarbonate converter have been proposed for the production of liquid compounds with low acidic HCO3- concentrations.

Conclusion: According to the findings, it is better to set up a program to reduce risk that the risk factor is not dangerous for us and it is recommended that we continue to do a good job of this study.

Keywords: Bicarbonate signal, sperm flagella and sperm motility

Investigation of the effect of Na + and H + converters on sperm motility in humans (Review)

Ali Ahmadi,[1,*]

1. Student, Faculty of Biological Sciences and Technologies, Islamic Azad University Sari Branch, Sari, Iran

Introduction: Introduction: Up to 15% of human couples are infertile and infertility in men is almost half of these cases. reach. Mammalian flagellum is a special type of motor fluid that is needed for sperm motility and male fertility. The effective movement of the flagellum depends on the axonal function, which in turn depends on the appropriate ion homeostasis in the flagellum chamber. The aim of this study was to investigate the effect of Na + and H + converters on sperm motility in humans

Methods: Methods: This study was conducted in 1399 by searching for keywords such as Na +, H + converters and sperm motility in humans in reputable databases such as: pub med and google scholar. Finally, 15 articles were found from These 15 articles used 10 articles

Results: Results: Based on the studies obtained from the articles, the results show that physiologically, sperm is of great importance in terms of motility, maturity and acrosome reaction, which maintains the pH of sperm through the involvement of several mechanisms among them with sodium-hydrogen converters. . They are also integrated membrane proteins that exchange sodium + hydrogen. All of these physiological processes are possible due to the micro-orchestrated signaling pathways between skeletal protein complexes and plasma membrane elements, such as ion channels and carriers. Disruption or regulation of these proteins can lead to ciliary motility impairment. In this study, we reviewed recent advances in ion channel function and transport and related signaling pathways in human sperm parasites. Pathological and pharmacological studies of specific ion channels of sperm in species that can (For example, empty mice) provide clear evidence of the role of the canal in sperm physiology and ultimate fertilization. In this study, sodium-hydrogen exchangers were shown to be essential for sperm function because They cause infertility due to severe defects in sperm motility

Conclusion: Conclusion: According to the findings, it is better to set up a program to reduce risk that the risk factor is not dangerous for us and it is recommended that we continue to do a good job of this study.

Keywords: Na +, H + converters and sperm motility in humans

Investigation of the toxicity of quinolone anticancer drug, levofloxacin, on bone marrow hematopoietic stem cells (Research Paper)

Azra Rabbani - Chadegani,[1,*] Melika Zamanian,[2]

1. Institute of biochemistry and biophysics at Tehran University
2. Institute of biochemistry and biophysics at Tehran University

Introduction: One of the most common side effects of anticancer drugs is on bone marrow. Disruption on hematopoietic stem cells located in the bone marrow, due to their importance in hematopoiesis, leads to defect in the immune system, blood supply to tissues, and blood clotting. Quinolones are a group of antibiotics studied extensively as anticancer drugs. They can stimulate apoptosis, inhibit cell proliferation and metastasis, hence the use of these drugs as antibiotics or anticancer drugs is associated with several side effects. To date, the effect of levofloxacin on bone marrow has not been studied, therefore, the aim of this study was to investigate the cytotoxic effects of levofloxacin on bone marrow hematopoietic stem cells (HSCs) to determine the appropriate dose of the drug and to identify the mechanism of its action on these cells.

Methods: Non-adherent hematopoietic stem cells obtained from male Balb/c mice and cultured in DMEM medium containing 10% FBS in the presence of various concentrations of levofloxacin. Trypan Blue, MTT, Fluorescent staining, Flow cytometry, Western blot and qRT-PCR tests were used in this research.

Results: The results showed that the toxicity of levofloxacin on HSCs is dose- and time-dependent in which after 18 h IC50 was 275 µM. Also, fluorescent staining and flow cytometry were indicated that apoptosis increased via increasing toxicity. Content and mRNA expression of HMGB1 protein were decreased by increasing concentration of Levofloxacin, However HMGB1 release into the cell culture media increased suggestively apoptosis has been enhanced. In addition the content and mRNA expression of BCL-2 protein was decreased and content of caspase-3 protein was increased.

Conclusion: From the results is concluded that levofloxacin induces apoptosis in HSCs of bone marrow cells through HMGB1 protein and BCL-2, suggesting that it can be employed in alone or combination therapy to minimize anticancer drugs toxicity.

Keywords: Levofloxacin, bone marrow hematopoietic stem cells, side effects, cancer, apoptosis.

Investigation pain modulatory effect of isoniazid by formalin test in male rats (Research Paper)

Amir Abbas Barzegari,[1,*] Maryam Azaddar,[2] Babak Vahdani,[3] Saeed Khalili,[4]

1. Assistant Professor of Animal physiology, Department of Biology, Faculty of Basics Sciences, University of Maragheh, Maragheh, Iran.
2. Instructor of Animal physiology, Department of Biology, Faculty of Basics Sciences, University of Maragheh, Maragheh, Iran.
3. Master of Science (MSc) student in Microbial Biotechnology, Department of Biology, Faculty of Basics Sciences, University of Maragheh, Maragheh, Iran.
4. Master of Science (MSc) student in Microbial Biotechnology, Department of Biology, Faculty of Basics Sciences, University of Maragheh, Maragheh, Iran.

Introduction: The transmission and perception of pain are complex processes involving both the central and peripheral nervous systems. In general, pain impulses are generated, propagated, and sustained by the liberation of various autocoids, ions, and neurotransmitters at various points between the site of tissue damage, along the afferent sensory fibers, and within the spinal cord and brain. One of the most important inhibitors of pain is the GABAergic system. Isoniazid is a drug of choice as a first-line defense against active and latent tuberculosis. It is also involved in pain modulation in high doses by decreases the GABA levels of the brain. However, some studies showed that low-dose isoniazid has GABA-elevating effects.

Methods: In order to study the antinociceptive effects of IP injection of Isoniazid male Wistar rats (200-270 g) was performed. Isoniazid (25, 50, 75 mg/kg, IP) was administered 60 minutes prior to formalin injection (50 µl of 4%). Then, formalin-induced paw jerking, and licking behaviors were recorded for 1 h.

Results: The results of current study showed that Isoniazid (25, 50 mg/kg, IP) did not have any significant effects on flexing duration in the first phase but could significantly reduce it in the second phase of the formalin test ($P<0.05$, and $P<0.001$, respectively). While 75 mg/kg of Isoniazid (IP) significantly reduced flexing duration in the both first ($P <0.05$) and second ($P<0.001$) phases of formalin-induced pain.

Conclusion: Consequently, the revealing results showed that 75 mg/kg of Isoniazid has an antinociceptive effect on behaviors in both the first and second phases of the formalin test, and it could consider as the effective dose for future formalin-induced pain studies.

Keywords: Isoniazid, Pain, Formalin test, Analgesia.

involvement of interferon gamma+874 A/T polymorphism in the pathogenesis of and Therapeutic Response to Immune Thrombocytopenia (Research Paper)

Mehran Amrovani,[1,*] Hadi Rezaeeyan,[2] Najmaldin Saki,[3]

1. Iranian Blood Transfusion Organization
2. Iranian Blood Transfusion Organization
3. Ahvaz jundishapour university of medical Science

Introduction: Immune thrombocytopenia (ITP) is an autoimmune disease characterized by symptoms of thrombocytopenia and bleeding due to production of autoantibodies against platelets. Recently, the occurrence of polymorphisms has been identified as one of the main causes of disease onset.

Methods: To conduct this study, we recruited 140 patients and control individuals with no history of platelet loss. After collection of specimens, the prevalence of interferon-γ polymorphism was evaluated using the allele-specific oligonucleotide–polymerase chain reaction (ASO-PCR) technique and confirmed by sequencing techniques.

Results: The results showed that the frequency of the AA genotype was higher in the control group, compared with patients with ITP; however, in the acute and chronic groups, the frequency of the AT genotype was higher than that of the AA genotype. We also discovered that there was no significant correlation between platelet counts before and after treatment, nor in its related parameters with interferon (IFN)–γ polymorphism.

Conclusion: rs2430561 does not seem to have any role in ITP pathogenesis and treatment response.

Keywords: IFN-γ polymorphism, immune thrombocytopenic purpura, platelet, pathogenesis, treatment

Is it possible that the human body also has a factory? (Review)

mahdi rafati,[1,*] kasra kamani,[2]

1. Dr. Mohammad Shafiee's High School
2. Dr. Mohammad Shafiee's High School

Introduction: Hepatic metabolism is performed in different ways, such as: oxidation, reduction, hydrolysis. The purpose of the liver in doing this is to facilitate the excretion of the drug, which if the drug is dissolved in water will be easily excreted through the kidneys. Metabolism enzymes are present in all parts of the body but are highly concentrated in the liver. People's hepatic metabolism is very different ‹In some people, hepatic metabolism occurs so rapidly that the amount of drug does not reach its therapeutic value at the target site, so the drug is ineffective in some people. Conversely, in some people, the liver metabolism is so low that most drugs in therapeutic doses cause poisoning in these people. Factors involved in hepatic metabolism include genetics, chronic Liver disease, heart failure, and drug interactions.

Methods: Hepatic metabolism is performed in different ways, such as: oxidation, reduction, hydrolysis. The purpose of the liver in doing this is to facilitate the excretion of the drug, which if the drug is dissolved in water will be easily excreted through the kidneys. Metabolism enzymes are present in all parts of the body but are highly concentrated in the liver. People's hepatic metabolism is very different ‹In some people, hepatic metabolism occurs so rapidly that the amount of drug does not reach its therapeutic value at the target site, so the drug is ineffective in some people. Conversely, in some people, the liver metabolism is so low that most drugs in therapeutic doses cause poisoning in these people. Factors involved in hepatic metabolism include genetics, chronic Liver disease, heart failure, and drug interactions.

Results: The main function of the liver is to filter the blood from the gastrointestinal tract before transferring it to the rest of the body Slowly More than one liter of blood is filtered through the liver every minute. The liver is also a substance The chemical breaks down and metabolizes toxins. The liver maintains the balance and regulation of the body's hormones Plays a role. The liver also makes important proteins for blood clotting. Liver location Blood glucose storage. The liver converts glucose into glycogen and stores it. If necessary, it converts glycogen back to glucose and enters the bloodstream. Liver

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also a substance The chemical breaks down and metabolizes toxins. The liver maintains the balance and regulation of the body's hormones Plays a role. The liver also makes important proteins for blood clotting. Liver location Blood glucose storage. The liver converts glucose into glycogen and stores it. If necessary, it converts glycogen back to glucose and enters the bloodstream. Liver

Keywords: liver health

Is leukemia inhibitory factor involved in the pathogenesis of preeclampsia? (Review)

Mehrnaz Abdolalian,[1] Parvinsadat Eslamnik,[2,*]

1. Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Iranian Blood Transfusion Organization (IBTO), Tehran, Iran
2. Department of Obstetrics and Gynecology, School of Medicine, Yasuj University of Medical Science, Yasuj, Iran.

Introduction: Preeclampsia (PE) is a pregnancy-specific disorder characterized by high blood pressure after the 20th week of pregnancy and other organ disorders such as kidney failure, liver involvement, neurological and hematological complications in the mother's body. The etiology and pathogenesis of this disorder remain unknown. Leukemia inhibitory factor (LIF) is a secretory glycoprotein of the IL-6 super family. LIF has various functions in fetal development, embryo implantation in the uterus and inflammatory responses. Due to the role of this factor in the process of pregnancy and fetal development, In this study, we first reviewed the role of LIF in the pathogenesis of PE through PE-related pathways such as inflammation, hypertension and endothelial dysfunction.

Methods: This review article is a study of PubMed content from 1980 to 2020. The keywords used in this search were -Leukemia Inhibitory factor-, -Preeclampsia-, -Endothelial Cell Dysfunction-, -Inflammation- and --Hypertension-.

Results: JAK / STAT is one of the pathways activated by LIF .Binding of LIF to LIF receptor (LIFR) via the JAK/STAT3 signaling pathway and up-regulation of MMP-14 increases endoglin production. Increased endoglin levels due to increased MMP-14 expression are involved in Endothelial dysfunction. Damage to the maternal endothelium has been considered as the main hallmark of PE . Phosphorylation of STAT3 by binding LIF to LIFR leads to abnormal expression of ICAM-1 and VCAM-1 on the surface of Endothelial cells, leukocyte excitation, induction of inflammation and endothelial dysfunction. Binding LIF to LIFR via the JAK / STAT pathway also activates RhoA. RhoA inhibits eNOS(endothelial nitric oxide synthase) phosphorylation and decreases NO (nitric oxide) production. If the production of NO (as a vasodilator) is impaired, it is involved in the pathogenesis of many diseases such as hypertension and PE. The level of angiogenic factors such as VEGF(vascular endothelial growth factor) decreases in PE. There is evidence for the effect of LIF on decreased VEGF gene expression.

Conclusion: Given that PE is one of the leading causes of mortality during pregnancy in pregnant women, the study of factors affecting the pathogenesis of PE is very effective in achieving therapeutic methods. It seems that the binding of LIF to LIFR can induce inflammatory responses, hypertension and endothelial dysfunction (as the main hallmark of PE) by inducing different signaling pathways, especially the JAK/STAT3 pathway.

Keywords: Leukemia inhibitory factor, Pathogenesis, Pre-eclampsia.

Isolation and characterization of aquatic bacteria from the cold water of Mount Sabalan (Research Paper)

tahereh ebrahimi,[1] vahideh tarhriz,[2,*]

1. Department of Nano-Biotechnology, Pasteur Institute of Iran, Tehran, Iran
2. Molecular Medicine Research Center, Biomedicine Institute, Tabriz University of Medical Sciences, Tabriz, Iran

Introduction: Background: Cold environments are effectively inhabited by a large number of different psychrophilic bacterial species. The psychrophilic bacterial strains from these environments are a good supply for cold-active enzymes like proteases, amylases and lipases having industrial appliances especially in medical and pharmaceutical industries. Sabalan (Savalan) Lake is a stable crater lake locating at the summit of Sabalan. The biodiversity of microbial flora in this area needs to be explored to find its similarity with arctic regions biodiversity. Objective: The psychrophilic bacterial population of Sabalan (Savalan) Crater Lake was identified. The current research is the first report of aquatic bacterial strains isolation and characterization from Sabalan Lake.

Methods: Water sample collections were cultured on four different media and colonies were isolated by the plating method. The phylogenetic features of isolates were examined and the phenotypic characteristics were investigated using specific culture methods.

Results: The results of morphological tests indicated that most isolates were Gram-negative and rod shape, which were able to grow between (-4)-(+37) ºC. The phyligenetic analysis revealed that the isolated strains belong to Pseudomonas, Yersinia, Kocuria, and Micrococcus genera and about 60% of the isolates belong to the various species of Pseudomonas as a dominant genus with abounded frequency

Conclusion: It can be concluded that the same cold environmental condition of these areas has the same microbial diversity with the same ancestors, while the geographical distances are so extensive.

Keywords: Sabalan (Savalan) Crater Lake, Pychrophilic Bacterial, Yersinia sp., Pseudomonas sp.

Isolation and rapid screening of emetic toxin producing Bacillus cereus strains in foodstuffs based on groEL, ces, and cer genes, using an improved Polymerase chain reaction assay (Research Paper)

Esmaeil Ghorbanalinezhad,[1,*] Donya Jodairi Mojaveri,[2]

1. Faculty of Department of Microbiology, Islamic Azad University of Tonekabon branch, Tonekabon, Iran
2. Master student of Microbiology, Islamic Azad University of Tonekabon branch, Tonekabon, Iran

Introduction: Bacillus cereus is a rod shape spore forming gram positive bacterium. This bacterium known as cosmopolitan food born poisoning agent. Many of Bacillus cereus strains causes diarrhoeal and emetic form of food poisoning. Diarrhoeal diseases causes by haemolytic and nonhaemolyic enterotoxins such as Hbl and Nhe Respectively, and Cytotoxin K. Emetic type of diseases causes by emetic toxins that coded by the responsible genes such as groEL, cer, and ces. The aim of this research was isolation and rapid screening of emetic toxin producing Bacillus cereus strains in foodstuffs based on groEL, ces, and cer genes, using an improved polymerase chain reaction assay.

Methods: In this descriptive-cross sectional study, 10 samples of homemade and restaurant cooked rice was collected. Then cultural and biochemical characterestics and antibiotic resistance pattern of Bacillus cereus isolates were studied by disc diffusion(Kirb- bauer) method. In molecular survey, the DNA of Bacillus cereus was extracted and the presence of emetic toxin causing genes were studied by PCR method.

Results: Of all the cooked rice samples that were examined, isolates of Bacillus cereus was obtained and emetic toxin producing genes (groEL, ces, and cer) in isolates were proven. Of ten isolates, there were 4, 2, and 4 positive samples relative to the genes of groEL, ces, and cer, respectively, in isolated Bacillus cereus strains. Results revealed that the samples have emetic toxin producing genes (groEL, ces, and cer) but the frequency of genes in isolates were not the same.

Conclusion: Use of PCR method for rapid screening of emetic toxin producing Bacillus cereus strains in Foodstuffs is a convenient method until to ensure the health of consumable food. Increasing information about the causes of food poisoning can reduce the incidence of this complication. The results of this study can be useful in obtaining information about the heaith of foods specially cooked rice, as well as the basis for further studies, including the pathogenesis mechanisms of Bacillus cereus.

Keywords: Bacillus cereus, emetic toxin, groEL, ces, cer genes

Knowledge Domain and Emerging Trends in Oral Cancer: A Scientometric Analysis Based on Iranian Publications (Review)

Maryam Zarei,[1] Golbarg Mehdizadeh,[2] Yasaman Mashayekhi,[3] Raheleh Chamanro,[4] Arash Ghazbani,[5,*]

1. Student Research Committee, Bushehr University of Medical Sciences, Bushehr, Iran.
2. Student Research Committee, Bushehr University of Medical Sciences, Bushehr, Iran.
3. Student Research Committee, Bushehr University of Medical Sciences, Bushehr, Iran.
4. Student Research Committee, Bushehr University of Medical Sciences, Bushehr, Iran.
5. Student Research Committee, Bushehr University of Medical Sciences, Bushehr, Iran.

Introduction: Cancer of the oral cavity is the 11th most common malignancy in the world and is associated with low survival. Oral cancer has been reported as one of the top ten cancer types in Iran. Although important knowledge has been gained about oral cancer, current results from published documents are still under debate. Therefore, this research conducted to review the scientific progress of oral cancer via a scientometric evaluation to identify the future perspectives.

Methods: In order to retrieve reliable data, Web of Science (WoS) database considered as the data source of the present study. Our search strategy contained keywords that were associated with oral cavity-related cancers which were selected from Medical Subject Heading (MeSH). Regarding the time of data collection, the timespan limited to all documents published before 2021 with at least one author affiliated to Iranian organizations. Bibliometric parameters at the level of documents and authors were assessed. Co-occurrence network analysis and visualizations were performed by VOSviewer v1.6.15.

Results: A total of 310 documents were retrieved from WoS. Original articles (75.48%) and reviews (15.80%) were the most common document types for Iranian publications. In total, documents on oral cancer by Iranian authors received 3015 citations. In results, the average citation per document was 9.83 (H-Index=27). Among Iranian authors, Khademi B. with 14 (4.51%), Kordi-Tamandani DM., Mohtasham N., and Shakeri MT, with 9 (2.90%), and Alaeddini M. with 8 (2.58%) documents were the most prolific researchers by the number of publications. A review on journals indexed in WoS showed that among the journals hosting publications related to Oral cancer by Iranian researchers, Asian Pacific Journal of Cancer Prevention published the most

significant number of documents 17 (5.48%). The co-occurrence network for keywords represented 4 publication clusters. The largest cluster was related to studies on pathological aspects of oral cancer, followed by epidemiological studies.

Conclusion: The present investigation showed that Iranian researchers have covered a wide range of oral cancer-related areas. Although a large number of research projects on oral cancer were epidemiological and pathological evaluations, it seems that oral cancer research in Iran is switching toward genetical, cellular and molecular investigations (such as investigations on miR-100 and miR-125b expression) as well as research on oral cancer possible treatments. Based on the present results it is not unpredictable that research on oral cancer biomarkers and also, clinical research continue during future decades.

Keywords: Oral Cancer, Oral Neoplasm, Scientometrics, Bibliometrics, Co-occurrence Network

knowledge of sexually transmitted infections(STI) in youth (Review)

hanane hamidi,[1,*]

1. Undergraduate nursing student, Khalkhal university, Iran

Introduction: Sexually transmitted infections (STIs) are a serious health care problem in the world, both in industrialized and in developing countries, they are increasing among youth and can cause acute and chronic disease also social and economic problems but most of them are preventable and treatable.

Methods: 20 articles published between 2018 and 2021 were selected in PubMed and reviewed.

Results: Findings indicate that Knowledge of STI was the low and major source of information was from movies and the internet and associated with age, level of education, employment status, attitude, the country they lived and preventive practices of the respondents. Developing countries undergo a great burden. In Islamic societies, sexual issues are sensitive and rarely discussed. Significant positive associations were shown between knowledge of safe sex by youth living with other people, those who had studied family planning and had religious beliefs reflecting acceptance to using birth control. HIV was the most known than other STIs. Some studies found that males had better knowledge than females the observed difference was not statistically significant. some studies showed that those with less knowledge had a higher risk of sexual behaviors.

Conclusion: young people had low knowledge about STIs in most studies, It is necessary to emphasize youth as the most vulnerable group. Increasing the awareness of STI starting from school age may help young people to live healthier and we need media campaigns to teach young adults who do not attend university or school.

Keywords: Knowledge, STI, youth

Laboratory animals in biomedical research: ethical concerns (Review)

Faezeh Tolouei,[1,*] Danial Safarpoor,[2]

1. Department of Genetics, Faculty of Basic and Medical Sciences, Islamic Azad University, Science and Research Branch, Zanjan, Iran
2. Faculty of Veterinary Medicine, Islamic Azad University, Karaj Branch, Karaj, Iran

Introduction: Laboratory animals have been used in experimental research to increase our knowledge in biological and biomedical fields. Increased concern for animal rights requires a greater focus on the ethical issues. Also, the reliability of the results of these studies will depend on the use of correct design and implementation methods.

Methods: This study has benefited from digital libraries resources published from 2005 to present.

Results: Studies in Iran show that despite improving the laboratory animals care status and increasing the awareness of researchers working with laboratory animals, many researchers are still unfamiliar with the ethical codes and standard operating procedures for working with laboratory animals. All biomedical research projects involving laboratory animals must be submitted and reviewed by ethics committees. The guiding principles of the 3Rs (Replacement, Reduction and Refinement) underpin the humane use of animals in biomedical research and must be used properly by researchers. All researchers must take the necessary training course(s) in working with laboratory animals and obtain certification. Every researcher must have a thorough understanding of the biology and behavior of the laboratory animal used. Researchers must also be inform of the importance of the work being done, and consider all the necessary preconditions based on the available scientific background. Supervisory committees must monitor the proper implementation of the instructions throughout the research projects.

Conclusion: The use of animals in biomedical research must be based primarily on ethical assumptions, and must certainly justify the use of animal.

Keywords: Laboratory animal, ethics, biomedicine, research

LDL-C estimation by Sampson's equation in an Iranian population

(Research Paper)

Asma Kheirollahi,[1,*]

1. Department of Comparative Biosciences, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran

Introduction: Today, the use of calculation methods for LDL-C estimation is common in many clinical laboratories, particularly in developing countries. Recently, Sampson et al. developed a new equation for LDL-C estimation in 2020. However, its accuracy has not been assessed in varied populations, including Iranians. The aim of this study was to compare the LDL-C calculated by the Sampson equation with the measured LDL-C by direct homogeneous assay over a wide range of TG in Iranian subjects.

Methods: A data set of 2752 subjects were enrolled in the study. All samples were analyzed in terms of lipid profiles using a direct homogeneous assay. For each subject, the LDL-C was calculated using the Sampson equation: LDL-C=TC/0.948−HDL-C/0.971−(TG/8.56+TG×non-HDL-C/2140−TG2/16100)−9.44.

Results: Although calculated LDL-C by Sampson equation showed a good correlation with the direct LDL-C, the mean difference between Sampson-estimated LDL-C and the directly measured LDL-C was significantly different. Moreover, the Sampson equation indicated the best performance in TG > 3.39 mmol/L subgroups. However, it showed LDL-C overestimation for TG < 3.39 mmol/L ranges.

Conclusion: It seems that the Sampson equation has appropriate performance in the setting of hypertriglyceridemia in the Iranian population.

Keywords: LDL-C; Sampson equation; Hypertriglyceridemia

Leukocytes Parameters, CRP, and Ferritin in Iranian Patients with COVID-19 Infection; A Cross-sectional Study (Research Paper)

Gevik karpians ,[1,*] Vahhab Piranfar ,[2]

1. medical group
2. medical group

Introduction: Coronavirus disease known as COVID-19 pandemic is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is affecting over 200 countries all over the world. This study was aimed to identify simple and swiftly available laboratory biomarkers to help facilitate effectual triage to categorize suspected COVID-19 patients.

Methods: According to a standard protocol, we collected clinical, etiological, and laboratory data of 140 patients who underwent diagnostic tests at Medical Laboratory Group, Tehran, Iran, from October 1 to November 28, 2020, based on PCR testing for SARS-CoV-2 infection. Leukocyte parameters, C-reactive protein (CRP) and, ferritin levels were measured in patients with positive PCR COVID-19 test.

Results: 140 patients with COVID-19 infection included in the study. The median age in women was 41.5 (23-60) years and 45.3 (22-68) years in men. Based on RT-PCR result, there were significant differences for neutrophil, lymphocyte, and monocyte counts. Overall, 72.8% of patients had monocyte count more than 11 ×109 /L. The mean neutrophil lymphocyte ratio (NLR) for women was 2.8 (SD: 1.8) and 2.6 (SD: 1.7) for men. Only in 15 patients (10.7%) with respiratory symptoms, CRP level was more than 5 mg/L.

Conclusion: We found a significant increase in monocyte count. Lymphopenia was also observed. In patients with respiratory symptoms, CRP was significantly higher than the normal reference range.

Keywords: Acute respiratory distress syndrome, Coronavirus, Cytokine release syndrome, Lymphopenia,

Long non coding RNA : Potential players in cardiotoxicity induced by chemotherapy drug (Review)

Mehran Amrovani,[1,*] Mohmmad Javad Mohammadtaghizadeh,[2] Mahsa Karimzadeh Aghaali,[3] Somayeh Zamanifard,[4] Arash Alqasi,[5] Mozhdeh Sanaei,[6]

1. Iranian Blood Transfusion Organization
2. Atherosclerosis Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
3. Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran
4. Departement of Cardiology, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran.
5. Thalassemia and Hemoglobinopathy Research Center, Research Institute of Health, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
6. Medicine student, Student Research Committee, Faculty of medicine, Shiraz University of Medical Sciences, Shiraz, I. R, Iran.

Introduction: One of the most important side effects of chemotherapy is cardiovascular complications, such as cardiotoxicity. Many factors are involved in the pathogenesis of cardiotoxicity; one of the most important of which is long non-coding RNAs (lncRNAs). lncRNA has 200-1000 nucleotides. It is involved in important processes such as cell proliferation, regeneration and apoptosis; today it is used as a prognostic and diagnostic factor. Also, various drugs by acting on lncRNAs can affect cells. Therefore, by accurately identifying lncRNAs function, we can play an effective role in preventing the development of cardiotoxicity induced chemotherapy drugs, and use them as a therapeutic strategy to improve clinical symptoms and Increase patient survival.

Methods: Electronic databases, including EMBASE, PubMed and Scopus

Results: Different chemotherapy drugs can play effective role in drug-induced cardiotoxicity. Cardiotoxicity induced by chemotherapy drugs occurs following the aging of the heart muscle cells. Some actions occur during the process of aging, including: decrease cell proliferation, P53 and P16 proteins expression increment, decrease telomere length and telomerase activity. In these processes, lncRNA plays an important role as a regulatory molecule, so shutting down the lncRNA molecule plays a protective role against the aging of heart cells, and lead to drug-induced cardiotoxicity. In addition, lncRNA can induce toxicity in cells by inhibiting proliferation, inducing apoptosis, and producing reactive oxygen species (ROS). Thus, lncRNA via PI3K / AKT pathway can induce apoptosis and ROS production, and subsequently induce cell toxicity via Notch1 / KLF15 pathway by inhibiting cell proliferation .

Studies have also shown, that lncRNA can lead to Cardiovascular Disease (CVD) through toxin induction in cardiac muscle cells. Thus, lncRNA Cfast can trigger the TGF-β signaling pathway by inhibiting the interaction of COLT1 with the TRAP1 molecule; subsequently, by increasing the formation of SMAD2 / SMAD4 complexes, it induces fibrosis and finally toxicity in cardio myocytes, the product of which can be CVD induction. Also FOXD3-AS1 lncRNA can induce the phenomenon of Cisplatin chemoresistance by suppressing the miR-127-3P and increasing the MDM2 molecule expression. On the other hand, Drugs derived from Taxanes compounds such as Paclitaxel and Docetaxel as well as Adriamycin can reduce the proliferation of cancer cells by suppressing lncRNA MALAT1 and induce the effect of these drugs on these cells. Studies have shown that inhibition of ZEB1-AS1 lncRNA is required for the effect of Cisplatin on cancer cells. Inhibition of ZEB1-AS1 lncRNA in cancer cells leads to upregulation of miR-129-5P and subsequently inhibits cell proliferation and apoptosis induction in cancer cells through the inhibition of ZEB1 and bcl2 molecules. Considering the role of ZEB1-AS1 lncRNA in cell proliferation, including cardiac muscle cells, it is hypothesized that Cisplatin drug needs to inhibit ZEB1-AS1 lncRNA to induce its effect on cancer cells. Consequently, one of the side effects of this chemotherapy drug is probably cardiotoxicity; it happens by reducing the expression of ZEB1-AS1 lncRNA and inhibiting its function in the proliferation of cardio myocytes. Other Studies have also shown, that SOX2-OT lncRNA can intensify the induction of cellular apoptosis by Doxorubicin in cardio myocytes by targeting the miR-942-5P / DP5 pathway. Unlike SOX2-OT lncRNA, NEAT1 lncRNA by degrading miR-221-3P can prevent Doxorubicin-induced cardiac senescence in cardio myocytes; thereby it inhibits cardiotoxicity, whereas lncRNA SOX2-OT could be due to the effect of Doxorubicin inducing apoptosis in cardio myocytes. In addition Downregulation of lncRNA H19 can induce the effect of temozolomide on cancer cells by reducing the proliferation by suppressing the Wnt / β-Catenin pathway. on the other hand MT1JP lncRNA can induce the Cisplatin effect on cancer cells by inhibiting miR-24-3P and suppressing the Wnt / Beta-Catenin pathway in these cells. Due to the inhibitory role of this lncRNA in the cell proliferation, Cisplatin can lead to cardiotoxicity by inducing this lncRNA in cardio myocytes by inhibiting the cell proliferation. Also Expression of SNGH lncRNA can induce drug resistance to Sunitinib in the cancer cells through upregulation of CDCA3 molecule.

Conclusion: lncRNAs play an important role in the cardiotoxicity induced by chemotherapy drugs. Therefore, the identification of signaling pathways by lncRNAs that lead to the induction of cardiotoxicity by chemotherapy drugs can be used to design appropriate target therapies to minimize the cardiac complication of chemotherapy-related toxicity.

Keywords: Long Non-coding RNAs, Cardiotoxicity, Cardiomyocyte, Mechanism

Long non-coding RNAs and circular RNAs as potential biomarkers in hepatocellular carcinoma: A review study (Review)

Mohammad Hossein Donyavi,[1] Sadra Salehi-Mazandarani,[2] Parvaneh Nikpour,[3,*]

1. Department of Cell and Molecular Biology and Microbiology, Faculty of Biological Science and Technology, University of Isfahan, Isfahan, Iran
2. Department of Genetics and Molecular Biology, Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
3. Department of Genetics and Molecular Biology, Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

Introduction: Liver cancer is the sixth most common cancer in the world. Based on estimations, more than one million people will be diagnosed with liver cancer annually, by 2025. Hepatocellular carcinoma (HCC) accounts for > 90% of liver cancer patients. Since most of the HCC patients are diagnosed at advanced stages, the disease becomes incurable with poor prognosis. Therefore, new prognostic and diagnostic biomarkers for HCC are needed. Up to now, different types of RNAs have been identified to be dysregulated in cancers indicating their important roles. Long non-coding RNAs (lncRNAs) and circular RNAs (circRNAs) are two types of most commonly studied RNAs. LncRNAs are a group of non-coding RNAs with a length of > 200 nucleotides. They have roles in different cellular processes such as chromosome remodeling, transcription and intracellular trafficking. Abnormal expression of lncRNAs correlate with progression of cancer, tumorigenesis and metastasis. CircRNAs are a type of endogenous RNAs with single-stranded covalently closed loop structure without 5´and 3´free ends. Due to this closed structure, they are resistant to exonucleases. They can function as microRNA sponges, protein scaffolds and modulators of transcription. Studies revealed that both lncRNAs and circRNAs are differentially expressed and can utilized as prognostic and diagnostic biomarkers in HCC. In this study, we investigated these two RNA types as potential biomarkers in HCC.

Methods: In the current study, we searched in PubMed and Google Scholar to find relevant and the newest review and original articles regarding the subject and aim of the study.

Results: HCC is a global health challenge, therefore novel biomarkers to diagnose the disease at early stages and predict the prognosis of patients are needed. LncRNAs could be utilized as potential prognostic and diagnostic biomarkers and therapeutic targets in cancer. Various studies have indicated momentous lncRNAs in HCC. For instance, overexpression of HOTTIP, SNHG3 and FOXD2-AS1, and decreased expression of ELMO1-AS1 and NKILA as prognostic biomarkers represent poor prognosis of HCC patients.

Several studies show the importance of exosome-derived lncRNAs as candidate biomarkers in HCC. For example, the exosomal expression of three lncRNAs; ENSG00000248932.1, ENST00000440688.1 and ENST00000457302.2, as potential biomarkers, increase in HCC patients comparing with both chronic hepatitis patients and healthy volunteers. SPRY4-IT1, Linc00152 and UCA1, which have overexpressed in serum of HCC patients, can be mentioned as proper diagnostic biomarkers. One of the most studied lncRNA in HCC is HULC which is indicated as a strong diagnostic biomarker for HCC. This lncRNA is overexpressed in serum, exosomes and HCC tissues. CircRNAs have outstanding specialties including high stability and tissue-specific and developmental stage-specific expression patterns, and could be served as promising biomarkers in cancer. Studies have identified important circRNAs in HCC. For example, increased expression of circRHOT1, SCD-circRNA 2 and hsa_circ_104348, and decreased expression of circTRIM33-12 and circDLC1, as prognostic biomarkers, can predict poor prognosis of HCC patients. On the other hand, circRNAs as diagnostic biomarkers have been reported. Exosomal expression of hsa_circ_0004277 which is significantly increased in the plasma of HCC patients, has diagnostic value. Furthermore, hsa_circ_0004001, hsa_circ_0004123 and hsa_circ_0075792, which have increased expression in the HCC patient blood samples compared to healthy controls, separately or in a combination (with higher sensitivity and specificity), could be used as valuable diagnostic biomarkers. These studies have unveiled important lncRNAs and circRNAs which can be utilized as potential biomarkers for HCC in the near future.

Conclusion: long non-coding RNAs and circular RNAs could be served as novel prognostic and diagnostic biomarkers in HCC. In the current study, we tried to present a useful brief regarding these two RNA types as promising biomarkers in HCC.

Keywords: Hepatocellular carcinoma, Long non-coding RNAs, Circular RNAs, Biomarker

Low severity of COVID-19 in children, causes and hypotheses (Review)

Aida Mofazzal Jahromi,[1,*] Dorsa Gharehghooni,[2] Soha Azizi,[3] Rahil Mosallanejad,[4] Amir Abdoli,[5]

1. Student research committee, Jahrom University of Medical Sciences, Jahrom, Iran
2. Student research committee, Jahrom University of Medical Sciences, Jahrom, Iran
3. Student research committee, Jahrom University of Medical Sciences, Jahrom, Iran
4. Student research committee, Jahrom University of Medical Sciences, Jahrom, Iran
5. Zoonoses Research Center, Jahrom University of Medical Sciences, Jahrom, Iran

Introduction: In mid-December 2019, severe acute respiratory syndrome (SARS) caused by Coronavirus 2 spread worldwide. Fortunately, most children are asymptomatic or have mild disease and much lower mortality compared to adults. Here, we review Why does the coronavirus causes mild COVID-19 infection in children?

Methods: A systematic search was performed in four databases, including Scopus, PubMed, Science Direct, and ProQuest, to find original articles from 2021 using three main keywords such as COVID-19, mild symptoms, and children. Then, 297 studies were screened in 3 stages, and finally, thirty-two articles that met the eligibility criteria were selected.

Results: Based on the literature review, several factors were found that could explain the different severity of COVID-19 in adults and children. There are two types of angiotensin-converting enzyme 2 (ACE-2) in the body: soluble and in the membrane. ACE inhibitors and underlying disease in adults, by increasing the expression of ACE-2 membrane form, caused the virus to enter the cells more easily. Further expression of soluble ACE-2 in children acts as a neutralizing antibody and plays a protective role against COVID-19. ACE degenerates and inactivate bradykinin, that's more common in children, therefore symptoms like dry cough, decrease in oxygen saturation, and increased vascular permeability is reduced. Another pathophysiological mechanism of COVID-19 is damage to endothelial cells with SARS-CoV-2 penetration and subsequent inflammation and the creation of a prothrombotic environment that causes increased inflammation and clotting. Because children have healthy vasculature and less endothelial damage, they show milder symptoms. The age-related decline in ciliary cell function facilitates the passage of viruses into the lower respiratory tract. Increased ability of children to repair their lungs after infection, adult thymus atrophy and decreased T

cells, and increased sex hormones in adults are other reasons for the lower severity of the disease in children.

Conclusion: According to our conclusion, the most frequent hypotheses and reasons for the age-related difference in the occurrence of SARS-CoV-2 is the difference in the number of ACE2 receptors, and endothelial system physiology. Although the clinical manifestations of COVID-19 in children are less severe than adults, the disease may progress in them and these mild symptoms should not be ignored in them. It should also be emphasized that although children have mild symptoms, they are important vectors of the disease, so children vaccination is considered as a key COVID-19 pandemic-prevention strategy.

Keywords: COVID-19, mild symptoms, children

Low Vitamin D levels in both chronic hepatitis B patients and healthy controls: Findings from a study of North-East IRAN (Research Paper)

Aida Gholoobi,[1,*] Yasamin Alamian,[2] Mojtaba Meshkat,[3] Zahra Meshkat,[4]

1. 1 Medical Genetics Research Center, Mashhad University of Medical Sciences, Mashhad, Iran. 2Medical Genetics Research Center, Mashhad University of Medical Sciences, Mashhad, Iran; 2 Metabolic Syndrome Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
2.
3. Department of medical science, Mashhad Branch, Islamic Azad University, Mashhad, Iran.
4. Antimicrobial Resistance Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

Introduction: Hepatitis B is one of the most common infectious diseases worldwide. The present study aimed to evaluate the serum levels of vitamin D in patients with chronic hepatitis B infection and the control group.

Methods: This is a case-control study on 89 individuals infected with hepatitis B as a case group and 300 subjects who were not infected with HCV, HBV, and HDV and were replicated in terms of age and sex with the hepatitis B group. Serum levels of 25 (OH) D3 were measured as the main outcome in both case and control groups. Finally, all the data were analyzed along with demographic and related laboratory results of patients and healthy groups by SPSS software version 26.

Results: The mean age of subjects in the hepatitis B and control groups was 47.11 ± 13.26 and 47.89. 7.81 years, respectively (P = .6). Of 389 participants, 198 (50.9%) were male and 191 (49.1%) were female (p = .5). The mean serum level of vitamin D in the hepatitis B and control group was 24.98 ± 19.92, and 13.57 ± 7.77, respectively. The median serum level of vitamin D in the hepatitis B patients was significantly higher than that of the control group (P = .0001). In the hepatitis B group, 43.8% of patients had vitamin D deficiency, 38.2% of patients had insufficient serum vitamin D levels and 18.0% had sufficient vitamin D serum levels. Also in the control group, 80.7% of patients had vitamin D deficiency, 10.7% of patients had insufficient serum vitamin D levels and 8.7% had sufficient vitamin D serum levels (P = .001). Other results showed that there was no significant relationship between HBV viral load and serum levels of vitamin D (P = .88).

Conclusion: Based on the results, vitamin D deficiency was observed in both patients with hepatitis B and healthy individuals. This study has found that the median serum levels of vitamin D in hepatitis B patients were significantly

higher than that of the control group. Due to the lack of studies in this field in the world and in our country and contradictory findings, it seems necessary to conduct additional studies with a higher sample size in the future.

Keywords: 25 (OH) D3; HBV, Viral load, Chronic HBV

Magnetosome and Drug Delivery (Review)

Arezoo Hosseingholian,[1] Ladan Ahangari,[2,*] Bahareh Attaran,[3]

1. Al-Zahra University
2. Al-Zahra University
3. Al-Zahra University

Introduction: Magnetosomes are natural nanoparticles with a nucleus of iron oxide or iron sulfide derived from magnetotactic bacteria. This structure causes the ability of bacteria to move in the direction of the magnetic field. Since they are between 20 and 100 nanometers in size; and due to the membrane that exists around this iron nucleus, it creates a property for them to bind drugs and therapeutic agents, therefore by attaching the markers to their surface, the ability to precisely identify the target cell can be created in them; So, their use will be very effective in treating diseases such as cancer. This treatment can be by hyperthermia, drug delivery, gene therapy, or antibody delivery. Here is a summary of magnetosomes and a brief overview of the drug delivery using them as a method to treat cancer.

Methods: PubMed, Google Scholar, and Scopus were used for a comprehensive search for articles published up to 2020. Keywords were included magnetotactic bacteria, magnetosome, nanoparticles, cancer, and drug delivery. We chose the articles based on their title and abstract. Finally, we have found 61 Articles with our study criteria of selection.

Results: The use of MTBs and their characterization for biotechnological applications require a pure culture in vitro. This is not easy to achieve because MTBs prefer a low oxygen system. Their replication time is very long, which puts them at risk of contamination by fast-growing bacteria. Magnetococcus marinus strain MC-1 is used to transport drugs loaded on nanoliposomes in hypoxic regions of colorectal tumors in mice. The results show that when these nanocarriers are combined with bacterial magnetosomes, they improve treatment. The unexpected conclusion reached by scientist Felfoul and colleagues was that these bacteria were clinically safe; this discovery was surprising because safety features for a Gram-negative bacterium with a particular wall were not expected to be safe. In several studies, a set of DOX antitumor drugs and magnetosomes isolated from the MSR-1 strain using glutaraldehyde as a cross-transporter used in this set of one milligram of pure magnetosomes could be limited to 87 mg DOX. The relationship between magnetosome levels and DOX appears to be very stable, leading to more prolonged drug release. The activity of this complex against HLG0 and EMT-6 cell lines was evaluated in human leukemia and rat breast cancer, respectively. After 48 hours, it showed that 80% of the drug was bound to the magnetosome, and the drug was not

destroyed; In the systemic circulation, most DOX is not released before reaching the target, and it also showed potent antitumor activity. In another study, antitumor drugs cytarabine and daunorubicin were attached to magnetosomes using geaipin and polylactic glutamic acid. The prolonged-release time of these drugs indicates that they are used less for treatment.

Conclusion: The only problem with using magnetosomes is that they are limited compared to synthetic nanomagnets because synthetic nanomagnets can be made as much as needed, but magnetosomes are natural and depend on bacteria and their growth. Resolving this problem can be a turning point in the treatment of many diseases, especially cancer. Given that the growth of magnetotactic bacteria is long-term and grows better in low oxygen conditions, the use of appropriate antibiotics to prevent the growth of infectious microorganisms, as well as methods to accelerate the growth of bacteria, can be the first step to address these problems; Therefore, the use of artificial bacterial primary ecosystem can be a good option for a large-scale pure culture of these bacteria and increase growth efficiency. It is suggested that magnetosome technology be used to deliver high-dose drugs, such as antibiotics; As we see today that many antibiotics are ineffective due to uncontrolled use, then we can hope that the effective antibiotics will be able to neutralize the function of bacteria for a more extended period and be effective in specific diseases. It is worth mentioning that the use of magnetosomes to deliver drugs with severe side effects such as chemotherapy drugs and iodine therapy in various cancers, can reduce their negative effects rather, it can reduce the chance of recurrence of the disease and the numerous injections that make the condition difficult for the patient, both financially and in terms of health.

Keywords: Magnetotactic bacteria, Magnetosomes, Nanoparticles, Cancer, Drug delivery

Magnetosome and Hyperthermia (Review)

Ladan Ahangari,[1] Arezoo HosseinGholian,[2,*] Bahareh Attaran,[3]

1. Alzahra University
2. Alzahra University
3. Alzahra University

Introduction: Magnetosomes are natural nanoparticles with a nucleus of iron oxide or iron sulfide derived from magnetotactic bacteria. This structure causes the ability of bacteria to move in the direction of the magnetic field Since they are between 20 and 100 nanometers in size; and due to the membrane, that exists around this iron nucleus, it creates a property for them to bind drugs and therapeutic agents, therefore by attaching the markers to their surface, the ability to precisely identify the target cell can be created in them; So, their use will be very effective in treating diseases such as cancer. This treatment can be by hyperthermia, drug delivery, gene therapy, or antibody delivery. Here is a summary of magnetosomes and a brief overview of hyperthermia using them as a method to treat cancer.

Methods: PubMed, Google Scholar and scopus were used for a comperhansive search for articles published up to 2020. Keywords were included magnetotactic bacteria, magnetosomes, nanoparticles, cancer and hyperthermia. We chose the articles based on their keywords and abstract. Finally, we have found 64 Articles with our study criteria of selection.

Results: Loaded magnetosomes have a long-lasting release property that enhances the drug's effect to form a targeted magnetic therapy. Using doxorubicin (DOX), it has been shown that magnetosomes can provide gene therapy drugs.[56] About sixty years ago, Gilchrist et Al. recommended the use of hematite, 20 to 100 nm in diameter, using a magnetic field variable at 1.2 MHz to induce heat in the lymph nodes for treatment. The use of hyperthermia in the treatment of cancer is very attractive because it has no toxic side effects and therefore has fewer limitations than chemotherapy and radiotherapy, and even increases the efficiency of treatment, in which either the tumor disappears or its size may be reduced. It does not completely disappear, but inside the tumor, the temperature remains in the range of 37 to 45 degrees Celsius. [53] As mentioned earlier, due to the presence of a fat membrane around the magnetosome, the protein can attach to it, by which it detects specific cells and tissues. So, in any treatment that uses the magnetosome, damaged or cancerous tissue can form. And are an excellent alternative to SION therapy (Superparamagnetic Iron Oxide Nanoparticle synthetic particles used for hyperthermia) in hyperthermia. The use of an alternating magnetic field also allows the release of the drug to be controlled. [53], [60] Recently, poly-lysine-coated magnetosomes (PLLs) are more stable,

non-pyrogenic, and have a higher potential for heat generation, resulting in significant improvement and antitumor properties in intracranial tumors in mice. In this case, the temperature reaches 42 degrees Celsius in the tumor. [52] In one study, researchers compared the effect of using poly-lysine-coated magnetosomes (M-PLLs) and IONPs (compounds of an iron oxide core coated with hydroxymethyl starch) in hyperthermia to treat cancer. In this study, tumor volume change was measured as a function of time after administration of glucose (M-PLL) and IONPs to mice in different groups. [50] In another study, an experiment was designed to determine the location of M. gryphiswaldense (MSR-1) cells in vitro and the effect of hyperthermia treatment on lung cancer cells. Fluorescent staining can also be used to detect the correct placement of these magnetosomes on cancer cells. In one study, human A549 lung cancer cells were incubated for 4 hours in the presence of MSR-1 incubated using fluorescence. [61]

Conclusion: The only problem with using magnetosomes is that they are limited compared to synthetic nanomagnets because synthetic nanomagnets can be made as much as needed, but magnetosomes are natural and depend on bacteria and their growth.[53] Resolving this problem can be a turning point in the treatment of many diseases, especially cancer. Given that the growth of magnetotactic bacteria is long-term and grows better in low oxygen conditions, the use of appropriate antibiotics to prevent the growth of infectious microorganisms, as well as methods to accelerate the growth of bacteria, can be the first step to address these problems; Therefore, the use of artificial bacterial primary ecosystem can be a good option for a large-scale pure culture of these bacteria and increase growth efficiency. It is suggested that magnetosome technology be used to deliver high-dose drugs, such as antibiotics; as we see today that many antibiotics are ineffective due to uncontrolled use, then we can hope that the effective antibiotics will be able to neutralize the function of bacteria for a more extended period of time and be effective in specific diseases. It is worth mentioning that the use of magnetosomes to deliver drugs with severe side effects such as chemotherapy drugs and iodine therapy in various cancers, can reduce their negative effects rather, by not releasing it into the bloodstream, not destroying the drug, and maintain a reliable dosage of it for a long time, it can reduce the chance of recurrence of the disease and the numerous injections that make the condition difficult for the patient, both financially and in terms of health.

Keywords: Magnetotactic bacteria, Magnetosomes, Nanoparticles, Cancer, Hyperthermia

Male breast cancer spheroids respond differently to curcumin-loaded graphene nanosheets than MCF-7 spheroids (Research Paper)

Saeideh Jafarinejad Farsangi,[1,*] Seyede Elmira Yazdi Rouholamini,[2] zeinab Ansari asl,[3]

1. Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
2. Student Research Committee, School of Medicine, Kerman University of Medical Science, Kerman, Iran
3. Department of Chemistry, Faculty of Science, Shahid Chamran University of Ahvaz, Ahvaz, Iran

Introduction: Breast cancer (BC) in men is rare but the incidence rate is rising worldwide and the mortality of patients is still high. Unfortunately, the existing knowledge about MBC is so limited, and clinical strategies for the treatment of MBC are the same as those for female breast cancer (FBC). Graphene nanosheets with unique physicochemical properties have been considered as potential biomedical approaches for drug delivery, bioimaging, and therapy. Graphene oxide (GO) and graphene quantum dots (GQDs) are suitable nanocarriers for hydrophobic and low bioaccessible antitumor materials like curcumin. Here, we evaluated cell death in mammospheres derived from primary breast tumor cells from a man and MCF-7 in response to curcumin loaded on graphene nanosheets.

Methods: Mammospheres were exposed to graphene oxide-curcumin (GO-Cur) and graphene quantum dots-curcumin (GQDs-Cur) and the incidence of cell death was evaluated by Hoechst 33342/propidium iodide double staining and flow cytometry. In addition, the expression of miR-21, miR-29a, Bax, and Bcl-2 genes were assessed using RT-qPCR.

Results: We observed, GO and GQDs had no cytotoxic effect on Kerman male breast cancer/71 (KMBC/71) and MCF-7 tumor cells while curcumin-induced death in more than 50% of tumor cells. GO-Cur and GQDs-Cur synergistically enhanced the anti-tumor activity of curcumin. Moreover, GQDs-Cur induced cell death in almost all cells of KMBC/71 mammospheres (99%; $p < 0.0001$). In contrast, GO-Cur induced cell death in only 21 % of MCF-7 mammosphere cells ($p < 0.0001$). In addition, the expression of miR-21, miR-29a, and also Bax/Bcl-2 ratio did not follow the same pattern in KMBC/71 and MCF-7 mammospheres in response to GO-Cur and GQDs-Cur.

Conclusion: Although KMBC/71 and MCF-7 tumor cells had similar clinical features and displayed similar responses to curcumin, more investigations are

needed to clarify the detailed molecular mechanisms underlying observed differences in response to GO-Cur and GQDs-Cur.

Keywords: Breast tumor cells, Mammosphere, Curcumin, Graphene quantum dots, Graphene oxide

Manifestations of elements and minerals deficiency in the oral cavity (Review)

Hamideh Kadeh,[1] Shirin Saravani,[2,*]

1. Oral & Dental Disease Research Center, Department of Oral & Maxillofacial Pathology, School of Dentistry, Zahedan University of Medical Science, Zahedan, Iran
2. Oral & Dental Disease Research Center, Department of Oral & Maxillofacial Pathology, School of Dentistry, Zahedan University of Medical Science, Zahedan, Iran

Introduction: Nutritional deficiencies can affect all or part of the oral tissues such as teeth, periodontal tissues, salivary glands, mucous membranes and perioral skin. Elements and minerals play an important role in the balance of the body's normal metabolism, often in the form of cofactors.

Methods: An electronic search was conducted in Medline and Scopus limited to English language publications using key words Malnutrition, Minerals, Mouth, Oral pathology.

Results: Elements such as magnesium, calcium, and phosphorus in the diet are the main structural compounds in teeth. Also, calcium, zinc and iron are the most important elements with oral manifestations when deficient. Calcium deficiency is associated with an increased risk of periodontal disease and tooth loss. Fluoride in fluoridated water sources and toothpaste is associated with reduced tooth decay and enamel health. Iron deficiency is one of the most common diagnoses in the adult population, and the oral manifestations of iron deficiency are similar to those of B12 and folate deficiency, in which glossitis is a common finding. Recurrent aphthous stomatitis, as well as angular stomatitis and paleness of the oral mucosa due to anemia can also be other symptoms. Peripheral dermatitis in zinc deficiency thins the upper lip and takes on the appearance of a horseshoe shaped. Other symptoms of zinc deficiency may include flattened filiform papillae, impaired wound healing and xerostomia.

Conclusion: According to the Oral cavity may manifest early signs of nutritional deficiency, in this study, we discuss about oral manifestations due to deficiency of elements and minerals.

Keywords: Malnutrition, Minerals, Mouth, Oral pathology

MECOM/hsa-miR-4429/PSAT1 CeRNA axis affects Ovarian cancer development by regulating " MAPK signaling pathway" and " Glycine, serine and threonine metabolism": bioinformatics gene expression profiling and RNA interaction analysis (Research Paper)

MohammadReza Arbab,[1] Mohammad Rezaei,[2] Mansoureh Azadeh,[3,*]

1. Zist Fanavari Novin Biotechnology Institute, Isfahan, Iran
2. Zist Fanavari Novin Biotechnology Institute, Isfahan, Iran
3. Zist Fanavari Novin Biotechnology Institute, Isfahan, Iran

Introduction: Ovarian cancer is the sixth most common cancer and the fifth leading cause of cancer-related death among women in developed countries. Approximately 90% of human ovarian cancer arises within the ovarian surface epithelium (OSE). The vast majority of ovarian cancers are sporadic, resulting from the accumulation of genetic damage over a lifetime. Based on the latest studies, different risk factors could trigger Ovarian cancer, which among them the genetic biomarker such as miRNAs (micro-RNA) are considered to have essential impact on Ovarian cancer progression. In these decades, the competitive endogenous RNA (CeRNA) network can help us to detect valuable biomarkers and develop our knowledge about diagnosis cancers and treatment process. In cancer cells, the connection between the components of this network(levels of expression) changes (compared to the normal condition) and provides precious information about the disease and its stage.

Methods: First of all, GSE29450 raw data was selected from Gene Expression Omnibus (GEO) and analyze by Rstudio to obtain differentially expressed genes(DEGs). MECOM,PSAT1,CP and CD24 had remarkable expression. The most significant genes (|logFC| > 3 and adjusted p-value< 0.05) were selected and taken to miRWalk 2.0 to find a great number miRNAs. Furthermore, Venny 2.0 have been used and has-miR-4429 was identified as a mutual miRNA. To find decent lncRNAs, the miRNA was searched in LncBase v.3 and several lncRNAs were found which is called FTX,JPX,MALAT1,NEAT1. At last, Cystoscope software 3.8.2 was used to show the interaction between the components of the ceRNA network.

Results: After careful analysis of 10 clear cell ovarian cancer specimens and 10 normal ovarian surface epithelium (GSE29450), a total number of 394 differentially expressed genes (DEGs) were detected. DEGs with adjusted p-value < 0.05 and |logFC| > 3 were considered significant. 20 of the hub genes with the lowest adjusted p-value were taken to miRWalk 2.0. The miRwalk 2.0 database provided target miRNA for the chosen hub genes. Score and number of pairings were considered factors for a suitable miRNA. We identify the pathway of our hub genes by using Kyoto Encyclopedia of Genes and Genomes(KEGG). MECOM is present in an essential pathway for growth of

cell which is called MAPK signaling pathway and another gene, PSAT1 is present in Metabolic pathways and Biosynthesis of amino acids. The related genes to our miRNA which is named CP and CD24 are also have important rules in our cancer and they probably participate as the same as the two pathways which are mentioned above. Moreover, the KEGG 2021 Human database confirmed that PSAT1 is an essential part of Glycine, serine and threonine metabolism and CP involve in Ferroptosis pathway and MECOM in Lysine degradation.

Conclusion: Based on the above analysis, we identify CeRNA network between MECOM, PSAT1, and hsa-miR-4429 and FTX,JPX,MALAT1,NEAT1. Histone-lysine N-methyltransferase(MECOM) functions as a transcriptional regulator binding to DNA sequences in the promoter region of target genes and regulating positively or negatively their expression. Oncogene which plays a role in development, cell proliferation and differentiation. In addition, the participation of MECOM in a CeRNA network, as well as a signaling pathway, demonstrated the possibility of MECOM being a reliable biomarker for diagnostic and prognostic goals.

Keywords: ceRNA - Systems biology - Ovarian Cancer - Bioinformatics

Medical Biotechnology, Nano Dentistry (Review)

Reza Mohsen Beigi Tughraljerdi,[1,*]

1. Education

Introduction: Review: New technologies in medicine have created the possibility of great changes and developments. Today with the help of new sciences and New hardware and materials have revolutionized healthcare. A tooth is one of the organs of the body that is in As a result of their use, they are gradually worn out and need treatment and reconstruction. Humans from the beginning with dental diseases Has been confronted and has tried to resolve it. What we see today as dentistry is the result of the evolution of this field in History has been around for a long time and now this field is equipped with modern equipment and science and very advanced materials. Nanoscience As one of the new sciences in this field, it has had very important achievements. From time immemorial to the present day, the appearance of people and having attractive white teeth has been very important for all people and with Over time, this importance has taken on a growing trend. Due to the increasing progress of different public and use Emerging technologies such as nanotechnology in the majority of this public and related industries, today thinkers and thinkers The use of nanotechnology in the form of nanorobots, nanomaterials and various nanopowders produced in dentistry and in particular Teeth whitening and increasing their durability have begun and research in this area has begun. In this research to Nano applications in dentistry of silver nanoparticles using licorice and mint plants and their antimicrobial effect The title of the factor on tooth decay has been studied

Methods: Introduction: Significant advances in nanotechnology in recent years have been a highly advanced branch of research focusing on Use of molecular and atomic methods to create nanoscale products that may be used in the field Other sciences have also been discovered (.) Abiodun-Solanke I, 2014 The word -nano- comes from a Greek word for The meaning of -dwarf- is derived: a nanometer of very small size equal to dividing one meter by a billionaire (9-10 Meters). It's actually the size of a small glass ball compared to an object the size of Earth. Despite There is a small scale to nanotechnology, but it certainly has a lot of potential. The basic concept of nanotechnology It is based on the use of atoms and molecules to build functional structures. The first person to use this technology as a Richard Feynman, winner of the Nobel Prize in Physics, came up with an innovative research that could revolutionize science. He in In one of his lectures in 1959, he proposed the hypothesis that molecular machines have incredible Ability to build with atomic precision (.) Zdrojewicz Z, 2015 Nano-based treatment is undoubtedly one of the main areas Researchers in nanotechnology studies

are hoping that nanoscience can lead to advances in disease control Various conditions such as cancer or atherosclerosis. Each of the three main branches of nanotechnology (nanomaterials, molecular nanotechnology and Biotechnology) may become a source of invaluable discoveries and solutions in modern medicine .) Wojnicz, 2011 (to be Nanotechnology is based on structures that are ten thousand times smaller than the diameter of a human hair. Nanotechnology is not just research Makes it possible at the molecular level. Rather, it enables the fabrication of nanomaterials with new mesmerizing properties have. As a result, key nanotechnologies are one of the key technologies of the twentieth century, the century ahead. Innovative solutions to many medical and dental problems are to be found. Nano-containers used for topical pharmacy Powerful tools for effective treatment of side effects They are less negative. Implants and smart devices based on nanotechnology will conquer the market and dental treatments They will fundamentally change medicine, as has been the case in the field of materials science and medical imaging

Results: Conclusion Results of the study of the minimum inhibitory concentration (MIC) and the minimum lethal concentration (MBC) of these two types of nanoparticles on three Bacteria that cause tooth decay indicate that both types of nanoparticles have a growth inhibitory effect and a lethal effect on The bacteria in this study were. At low concentrations of nanoparticles, there was bacterial growth, but at increasing concentrations of nanoparticles, This led to a decrease in bacterial growth. Therefore, antibacterial effects are directly related to the concentration of biosynthetic silver nanoparticles Had. By examining the growth or non-growth of bacteria in culture medium containing different concentrations of nanoparticles, the minimum concentration Its inhibitor was identified. Comparison of the antibacterial effect of biosynthesized nanoparticles with two types of extracts shows that the antibacterial effect Bacterial nanoparticles biosynthesized with licorice extract on these bacteria, especially Streptococcus mutans are more numerous than other nanoparticles. Among the studied bacteria, resistance of Lactobacillus rhamnosus10 In contrast, more biosynthesized nanoparticles than Streptococcus and Actinomyces viscosus mutans reported. In the present study, silver nanoparticles were used using extracts of peppermint and licorice plants without the need to expend energy on raw materials. Expensive, were produced. Colloidal nanoparticles, and microscopically released microparticles; So to can even to Penetrate into bacterial cells and in this study, the nanoparticles produced have a good antimicrobial effect on oral bacteria The study showed; Therefore, based on their biological effects, the use of these nanoparticles can be used to fight infections It is effective due to the honey bacteria studied

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Keywords: Keywords: Biotechnology, Nano-Dentistry, Silver nanoparticles.

MELATONIN EFFECTS IN THE BREAST-CANCER AND ITS TREATMENT (Review)

Nima Ashouri,[1,*]

1. Imam Khomeini high school

Introduction: In recent years, cancer has become the first and most deadly disease in the world. Due to the causes and growth of cancer in humans, a significant increase in the incidence of this type of disease in the coming years is likely. Types of cancers with different processes, their effects on the body and the prognosis of this disease for treatment make it more difficult for researchers to work. The most common cancer among women is breast cancer.

Methods: Methods: the criteria for selecting were the articles that contained information about melatonin and breast cancer diseases and how to use melatonin in the treatment of these diseases Resources= -Melatonin and breast cancer: cellular mechanisms, clinical studies, and future perspectives- written by - v Stephen G. Grant, Melissa A. Melan, Jean J. Latimer, and Paula A. Witt-Enderbyr- . -Melatonin: an inhibitor of breast cancer written by - written by - Steven M Hill, Victoria P Belancio, Robert T Dauchy, Shulin Xiang, Samantha Brimer, Lulu Mao, Adam Hauch, Peter W Lundberg, Whitney Summers, Lin Yuan, Tripp Frasch, and David E Blask-.

Results: Melatonin actually has significant inhibitory effects in many cancers, specifically breast cancer. Melatonin has a vital role in almost every part of the occurrence and progress of tumor cells. Melatonin synergizes with chemotherapy and endocrine therapy to reverse drug resistance. Melatonin could be a therapeutic option for breast cancer. Melatonin has significant inhibitory effects in numerous cancers, especially breast cancer. In estrogen receptor (ER)-positive human breast cancer, the endostatin actions of melatonin are mainly achieved by suppressing ER mRNA expression and ER transcriptional activity via the MT1 receptor. Melatonin also regulates the transactivation of nuclear receptors, estrogen-metabolizing enzymes, and the expression of related genes. Furthermore, melatonin suppresses tumor aerobic glycolysis, critical cell-signaling pathways relevant to cell proliferation, survival, metastasis, and overcomes drug resistance. Studies in animal and human models indicate that disruption of the circadian nocturnal melatonin signal promotes the growth, metabolism, and signaling of human breast cancer, resulting in resistance to hormone therapy and chemotherapy, which may be reversed by melatonin.

Conclusion: in the last few years, a lot of research on melatonin as an anticancer agent has been published, and many studies from cell lines, animal models, xenografts in rodents, and human breast cancer cells have confirmed that melatonin inhibits the growth of breast cancer and induces apoptosis by mediating a large number of molecular pathways. Many of these mechanisms involve the activation of melatonin receptors, especially MT1. Moreover, melatonin synergizes with chemotherapy and antitumor treatments to reverse resistance, at least in part, to other treatments.

Keywords: melatonin, breast cancer,anti-cancer mechanism

Mesenchymal Stem Cells-Conditioned Medium; An Effective Cell-Free Therapeutic Option for in Vitro Maturation of Oocytes (Review)

Maryam Farzaneh,[1,*]

1. Fertility, Infertility and Perinatology Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Introduction: Infertility is a major reproductive health issue, worldwide. One of the main problems in infertile women is the failure to generate or release a mature egg. Therefore, the development of new technologies for in vitro generation or induction of mature oocytes can improve various ART procedures. Recently, stem cell-based therapy has opened a new window for several pathological complications. Mesenchymal stem cells (MSCs) are multipotent stem cells with the capacity to self-renew and differentiate into the mesodermal lineage. MSCs contains various bioactive molecules, which are involved in the regulation of key biological processes. They can secret multiple growth factors and cytokines to stimulate egg maturation. Although MSCs represent a promising source for cell therapy, the potential risk of tumor development reduced their clinical applications.

Methods: Recent studies have suggested that the supernatant or conditioned medium of MSCs also contains similar components and regulates the oocyte behavior. MSC-conditioned medium can eliminate the safety concerns associated with MSC transplantation and avoid rejection problems.

Results: MSCs have been shown to improve oocyte quality, ovarian function, and fertility.

Conclusion: Hereby, we summarized recent research findings of MSCs-derived conditioned medium in in vitro development of immature oocytes.

Keywords: Mesenchymal stem cells, Conditioned medium, Differentiation, Maturation, Oocytes.

Mesenchymal Stem Cells: A promising approach in COVID-19 treatment (Review)

Nima Abedini,[1] Mahtab Moghaddam,[2] Zahra Kakavand ,[3] Mahmood Talkhabi,[4,*]

1.
2. Department of Animal Sciences and Marine Biology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
3. Department of Animal Sciences and Marine Biology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
4. Department of Animal Sciences and Marine Biology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran

Introduction: With the spread of SARS-CoV-2 beyond the borders of Wuhan, the capital of Hubei province in China and the elevation of the status of covid19 to a pandemic, health systems, researchers and physicians around the globe were faced with an unpresented challenge. This virus like its predecessor SARS-CoV generally has respiratory manifestations. In most cases the patients show mild symptoms which usually require minimum medical intervention, however with an increase in age and the presence of comorbidities the symptoms might be more severe and even result in death. As cases grew worldwide, clinical manifestations went further than the respiratory system to include the nervous and cardiovascular systems. Current therapies for critically ill patients that are mostly concentrated on controlling inflammation in the acute phase of the infection, have some limitations. The therapy may be non- specific for SARS-CoV-2 or like remdesivir and Tocilizumab be difficult to obtain. Another important consideration is the long-term side effects of these treatments such as pulmonary fibrosis and ischemic damage to the lungs. In order to address these issues Researchers have turned to cell therapy because of their regenerative and reprogramming capabilities.

Methods: This study is a review, conducted by searching databases such as: Google scholar, PubMed, ResearchGate and Medline. 12 articles were chosen based on the keyword entries. Chosen articles fall into two categories: information and background on the subject and data on clinical trials.

Results: Current approaches in cell therapy include the use of mesenchymal stem cells (MSCs), induced pluripotent stem cells (iPSCs) and T-cells. Among these, MSCs are viable candidates for Covid-19 cell therapy for a multitude of reasons including easy interaction from several sources, multipotency and the ability to expand to desired clinical volumes in a short period of time. The uncontrollable secretion of pro-inflammatory cytokines in Covid-19 results in a phenomenon called a cytokine storm that leads to severe tissue damage

which can prove fatal and any effort in suppressing the immune system could derail the treatment process and be very dangerous. Mesenchymal stem cells possess anti-inflammatory features and are able to regulate the immune system by repairing damaged tissue. The systemic injection of mesenchymal stem cells results in their localization in the pulmonary vasculature; from there, these cells secrete anti-inflammatory cytokines, anti-microbial peptides, angiogenic factors and extracellular vesicles which improve pulmonary microenvironment, protect alveolar cells, prevent fibrosis and eventually improve lung function.

Conclusion: In this study, we have reviewed the latest findings and advances in Covid-19 mesenchymal stem cell therapy. Despite the production of several vaccines for Covid-19, a slow vaccination rate and the immergence of new variants highlights the importance of designing and developing specific therapies and treatments for controlling this disease. Cell therapy through mesenchymal stem cells has presented itself as a suitable candidate for the concentration of these endeavors. The potential for easy and non-invasive isolation and the possibility of long-term storage through cryopreservation are major benefits of this method. The success of pre-clinical trials shows great potential for this treatment.

Keywords: Covid19, Cell therapy , Mesenchymal stem cell, microenvironment, anti- inflammatory

Microbial fuel cells and applications in wastewater treatment (Review)

Farzaneh Dianatdar,[1] Zahra Etemadifar,[2,*]

1. University of Isfahan
2. University of Isfahan

Introduction: There are two general mechanisms for electron transfer in MFC: 1. Direct transfer electron or DET. 2. Mediated electron transfer or MET (11). One of the fields of research in MFC is power generation from wastewater along with the oxidation of organic or inorganic compounds. Any compound that can be destroyed by bacteria can be converted to electricity. The range of compounds includes acetate, glucose, starch, cellulose, wheat straw, pyridine, phenol, nitrophenol, and complex solutions such as household wastewater, desalination waste, waste leachate, chocolate industry waste, mixed fatty acids, and petroleum products (1). The MFC greatly reduces the amount of COD in the treated effluent. The highest percentage of carbon removal from wastewater with the help of the MFC is about 90% (12). Nitrogen removal from the wastewater is also possible by MFC. For example, the use of MFC for domestic wastewater treatment has reduced COD by 94% and nitrogen removal by 85% (13). Ieropoulos et al. (2012) identified urine as an excellent source of electricity generation in the MFC. In addition, Struvite crystals are extracted from the urine with the help of an MFC, and electricity is also generated (14). Recently, MFC has been used to remove sulfide by simultaneously generating electricity in wastewater treatment. In the anode chamber, sulfide was first produced with the help of sulfate-reducing bacteria and the sulfide is then converted to sulfur with the help of sulfide oxidizing bacteria (8). Provides oxidation/reduction conditions in MFC for the elimination of drugs, especially antibiotics (Sulfonamides, Penicillin, Sulfadimidine, aureomycin, Norfloxacin, Chloramphenicol) (15-16). MFCs have shown great potential for the reduction of heavy metals, which are used both at the anode as an electron donor and at the cathode chamber as an electron receiver (17). Yangpin et al. (2017), a single-chamber bio-photoelectrochemical system (BPES) that receives high-performance destruction for azo dye (methyl orange (MO)) and energy recovery (2). To improve wastewater treatment, technologies are added to the MFC, such as aerobic decomposition (AD), struvite deposition, algae treatment, and membrane filtration. In the first step, we have a settling tank to remove large particles. Then, depending on the characteristics of the wastewater, we have it through three different treatment ways: 1- Low organic load wastewater can be fed directly to the MFC system. 2- High organic load wastewater must be pre-fermented in an anaerobic reactor before entering the MFC system to produce biogas and the optimal composition for wastewater. 3. Phosphate-rich wastewater can undergo Struvite recovery before MFC treatment (18-19).

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Bioresource Technology. 2011;102(10):6304-7. 18. Li W-W, Yu H-Q, He Z. Towards sustainable wastewater treatment by using microbial fuel cells-centered technologies. Energy & Environmental Science. 2014;7(3):911-24. 19. .Fischer F, Bastian C, Happe M, Mabillard E, Schmidt N. Microbial fuel cell enables phosphate recovery from digested sewage sludge as struvite. Bioresource Technology. 2011;102(10):5824-30.

Results: MFC (Microbial Fuel Cell) is a system in which microbes oxidize organic matter and minerals, then transfer the generated electrons to the anode electrode, and then these electrons are transferred by wire to the cathode electrode, which generates electricity. Electron transfer from microbes to electrodes occurs in two direct and indirect ways (1). MFC has different types such as single-chamber and double-chamber and batch MFC (2). Of course, MFC has a variety of applications, such as generating electricity, treating wastewater, removing certain chemicals, biosensors, producing hydrogen, and using rumen bacteria (3-4-5-6-7-8-9). As the world's population grows, the need for energy has increased. The need for renewable energy and the reduction of environmental pollution in this system has received much attention. Water scarcity has led to many efforts to treat and use wastewater, and MFC is a suitable system for this. Reducing pollution is the most important task of wastewater treatment, but unfortunately, wastewater treatment processes are generally energy-intensive. During treatment, large amounts of greenhouse gases (GHG) such as carbon dioxide (CO2) and nitrous oxide (N2O) are released and disposal of activated sludge produced during the effluent treatment process is very difficult. In addition, many valuable resources such as phosphate (P4O3), ammonia (NH4+), and some metals in wastewater are not recovered, which is reduced by the MFC system.

Conclusion: MFC is a promising technology for sustainable wastewater treatment (WWT) combined with power generation. Investigation of complex interactions at the electrode and microbial interface increases the output power for practical applications in the MFC device. The description of the electrochemical mechanism in microbes has made considerable progress. However, more collaborative interaction in different disciplines is needed to make this technology more practical. Of course, there are currently many problems for this technology, such as low Colombic efficiency and internal resistance, etc., which should be further studied and researched.

Keywords: Bioelectricity, Microbial fuel cell, Molecular mechanism, MFC applications, Wastewater treatment

Microbiology meets machine learning (Review)

Fateme Yousef Saber,[1,*] Homa Keshavarz,[2] Sara Azima Haghighi,[3]

1. Department of Cell and Molecular Biology and Microbiology, Faculty of Biological Science and Technology, University of Isfahan, Isfahan, Iran
2. Department of Cell and Molecular Biology and Microbiology, Faculty of Biological Science and Technology, University of Isfahan, Isfahan, Iran
3. Department of Artificial Intelligence Engineering, Faculty of Computer Engineering, University of Isfahan, Isfahan, Iran

Introduction: Microbiology is defined as a scientific major focusing on small living creatures like bacteria, viruses, and fungi. Considering the fact that industrial manufacturing of essential products like enzymes, hormones, and medicines has attracted enormous attention, scientists are seeking the solution to develop sustainable approaches. Among all proposed green synthesis methods, microbial production seems to be the best option due to its fast, simple, and environmentally friendly production mechanisms.

Methods: The present article is a short review of how microbiology could benefit from machine learning algorithms. Various articles and books from Google Scholar and Pubmed database were used to gather this information using these keywords: microbiology, bioinformatics, and machine learning.

Results: Machine learning is a type of artificial intelligence in which computers will train rather than programmed to conduct specific tasks. Different algorithms counting Artificial neural network, Clustering, Decision tree, Gaussian process, K-nearest neighbors, Linear regression, Regularization, and Support vector machine/ regression have been widely used in different fields of microbiology: Analyzing Genomics, proteomics, and microarray data, evolution, and system biology. More specifically, machine learning has proved to be valuable in industrial strain development. Host strain selection, Metabolic pathway reconstruction, Tolerance enhancement, Metabolic flux optimization, Fermentation, and Downstream process are the well-studied subject in this area.

Conclusion: In line with industrial-scale production by microbes, it is essential to optimize crucial factors like temperature and pH. Applying computational modeling before conducting an experimental trial will provide a clear vision of how manipulating cellular and environmental factors would affect the process.

Keywords: microbiology, bioinformatics, machine learning

Microfluidic based-3D spheroid models for drug development studies: a review (Review)

Marziye Soleimani,[1,*] Zeinab Bagheri,[2]

1. Faculty of life science and biotechnology, Shahid Beheshti University, Tehran, Iran
2. Faculty of life science and biotechnology, Shahid Beheshti University, Tehran, Iran

Introduction: Monolayer or two-dimensional (2D) cell cultures are the primary test platform in biomedical research that supports conventional assays and high-throughput screening. In addition, 2D cell cultures are easy to use and very widespread, but cannot mimic the in vivo physiological state of natural tissues, so many of the results do not apply to clinical application. This lack of similarity between in vivo and in vitro conditions increases the cost and time invested in research, particularly in drug development studies. Research has shown, for example, that most cancer drugs that are effective in 2D cell cultures cannot work properly in the human body and yet less than 5 percent of the drugs reach the clinic. To overcome the gap, using animal models are common but they have some drawbacks such as being costly and time-consuming in addition to having physiological differences with humans. Subsequently, 3D cellular models have developed and attracted a lot of attention to narrow the gap between pre-clinical and clinical studies. Among 3D cell cultures, spheroids are one of the best cellular models especially for cancer research and solid tumor studies. They are widely used due to their diverse, easy, and cost-effective preparation methods. In recent years, microfluidic systems which can control the physiological condition and mimic the perfusion of metabolites and wastes by incorporating flow dynamics became an interesting alternative to traditional methods in 3D cell culturing. They are suitable platforms for spheroid cultivation or analysis.

Methods: Kwapiszewska et al. developed a microfluidic chip to culture tumor spheroids for in vitro drug screening. In their work, a microfluidic device by PDMS was designed and fabricated. The chip was composed of a concentration gradient generator (CGG) as a mixing channel which enables the formation of spheroids and analysis of drug screening results in a controlled fluid flow rate. After the device fabrication, HT-29 human colon carcinoma cells and Hep-G2 human liver carcinoma cell lines were cultured separately, and then their suspension was introduced to the microfluidic device using syringe pumps to form the spheroids. The drug screening was performed by long-term monitoring of the viability of spheroids exposed to different dosages of 5-fluorouracil (5-FU) drug. In another study, Lim et al. introduced a microfluidic spheroid culture device (μFSCD) for high-throughput cancer drug screening. their μFSCD has a concentration gradient generator

(CGG) for a parallel screening. After the formation of colon cancer cell (HCT116) spheroids in chip microwells, the drug (irinotecan) was injected into the device. Finally, live/dead Staining and Cell Viability Measurements were performed.

Results: The results from different spheroids which were exposed to different drug concentrations were collected and compared. This comparison can investigate drug efficiency. For instance, in the first research mentioned above, it was observed that low concentrations of 5-FU are more effective when the dose is repeated. Also, Lim et al. showed that the cell viability in different microwells containing more concentrations of irinotecan was lower and vice versa which was following the observations of spheroids roundness.

Conclusion: Using this combinational approach for drug development studies especially for nano-drug delivery to solid tumors is a new method to reduce the time and costs of preclinical researches, in addition, to reduce the gap between in vitro and in vivo studies. It's expected that a well-designed microfluidic-based spheroid culture system is a powerful tool for drug development researches as a 3D in vitro tumor model.

Keywords: Microfluidic systems; 3D cell culture; spheroid; drug development

Microfluidically Spun Microfibers for Cell-Therapy and Tissue Engineering Applications (Review)

Soheyl Mirzababaei,[1] Mona Navaei-Nigjeh,[2,*]

1. Pharmaceutical Sciences Research Center, The Institute of Pharmaceutical Sciences (TIPS), Tehran University of Medical Sciences (TUMS), Tehran, Iran
2. Pharmaceutical Sciences Research Center, The Institute of Pharmaceutical Sciences (TIPS), Tehran University of Medical Sciences (TUMS), Tehran, Iran

Introduction: Tissue engineering (TE) is a multidisciplinary approach that combines cell biology and engineering. TE aims to develop functional scaffolds outside of the human body that could replace damaged or dysfunctional tissues or organs. To fulfill this purpose, different bottom-up construction methods have been used to develop cell-laden structures in the form of fibers, droplets, and sheets with the functionality of the target tissue. Among these structures, fibers have gained attraction in the field of biofabrication and biomaterials since they can resemble the connective tissue and guide cell growth and network.

Methods: Several methods including wet spinning, rotary spinning, phase separation, and electrospinning have been used to develop microfibers. Among these, electrospinning is the most common method for fiber fabrication due to scalability and its capability to control the physicochemical properties of the fibers by changing the operational parameters. In this method, a high electric field will be subjected to a polymer solution that is fed to a needle in order to draw a fiber from the solution. This method yields in nonwoven or oriented mats. Meanwhile, due to the advances in microfabrication methods, microfluidic devices have been used for the fabrication of biomaterials. The microfluidic spinning approach consists of a sample flow which is a polymerizable solution, a sheath flow which acts as a lubricant to facilitate fiber extrusion and/or fiber formation, and a microfluidic device that provides a platform, in the channels of which the two fluids flow and come into contact to form the fiber. In this method, fibers form based on ion cross-linking, photopolymerization, solvent exchange, and chemical crosslinking.

Results: Although electrospinning is a simple method to fabricate fibers from a variety of polymers, it is not a suitable technique for generating cell-laden fibers. This is because the stress that is imposed on the cells could dramatically reduce their viability and functionality. In contrast, microfluidic spinning provides a more cell-friendly approach for the fabrication of meter-long cell-laden microfibers. By changing the properties of the sample flow, sheat flow, and the design of the microfluidic device, fibers with desirable physicochemical properties could be generated. Besides, fibers with different cross-sections could be tailored by changing the cross-section of

microchannels. Accordingly, cell-laden microfibers of desirable functionality could be produced. For instance, pancreatic islets could be encapsulated in microfibers for the treatment of type 1 diabetes mellitus. Grooved microfibers could be generated to guide the alignment of neural cells in order to generate neural conduits. Also by fabricating hollow fibers and encapsulating endothelial cells in them, microvessels could be generated to mimic vasculature in the human body.

Conclusion: Microfluidic spinning is a versatile approach that could fabricate microfibers with appropriate properties suiting a specific purpose. In this manner, not only could cells be seeded on the surface of the fibers, but also they could be encapsulated in the fibers to form functional hydrogel-based microfibers. The generated cell-laden microfibers could be used as artificial tissues to replace dysfunctional tissue in the human body. Besides, since they could provide a 3D structure that mimics the extracellular matrix, they could improve cell viability and functionality, therefore, be used as 3D in vitro models.

Keywords: Microfibers, Microfluidic spinning, Scaffold, Cell-laden tissue, Tissue engineering

Microfluidics: a powerful tool for producing a three-dimensional invasive tumor model (Review)

Parisa Poornemat,[1,*] Zeinab bagheri,[2]

1. Faculty of Life Sciences and Biotechnology, Shahid Beheshti University , Tehran, Iran
2. Faculty of Life Sciences and Biotechnology, Shahid Beheshti University , Tehran, Iran

Introduction: Invasive behaviors of cancer cells such as metastasis, angiogenesis, migration, and integration of cancer cells together are key factors in cancer mortality. These behaviors lead to the progression of cancer cells and make treatment more difficult. They can change the type and dose of the drug needed to treat cancer cells or affect the way the drug works, failing conventional therapies, increased mortality, and treatment costs. Therefore, identifying different aspects of these behaviors is very important in designing new drugs, choosing the right drug dose, drug delivery, and ultimately successful cancer treatment [2]. standard methods for evaluating cancer cells and testing drugs are animal models and two-dimensional cell culture. Animal models had limitations such as high cost and complete incompatibility with in vivo conditions [1,2]. Despite its advantages, such as reasonable cost and availability, two-dimensional cell culture, has the disadvantage of not mimicking cell-to-cell and cell-to-extracellular matrix interactions. In addition, growth signals are not available. As a result, three-dimensional cell culture systems are proposed that are very successful and reliable in pharmacological studies and understanding of cancer cells and can mimic cell interactions, provide uniform growth conditions for all cells, and distribute the environment evenly. 3D cell culture models are divided into two categories: liquid base and scaffold base [3]. Scaffold bases are obtained from synthetic or natural polymers and provide cell growth and extracellular matrix. 3D cell culture includes methods such as rotary cell culture, plate culture system, hanging drop culture method, and magnetic levitation method that can be used to create cells [4]. A Scaffold's independent model is spheroid tumors, which are self-assembling and capable of growing from single-celled suspensions. They also have morphological and physiological characteristics similar to cancer cells [4].

Methods: One of the most popular platforms for Assessment invasive behaviors is microfluidic chips. Microfluidic chips allow the control of nanoscale and microscale fluids and provide the conditions for biological processes that were very difficult to perform in the current cell culture model. The design of chips used to study the invasive behavior should allow observation of behaviors such as cell migration and metastasis. For example, Yan et al developed a microfluidic device to study the migration of cancer

cells to different organs. Their platform containing a porous polycarbonate membrane in the center, surrounded by two layers of PDMS containing a central well and five wells around them. For testing the chip, the cell suspension was poured into the central hole, then FBS and media were added to the system from under the membrane to evaluate migration [12].

Results: Truong et al. designed a microfluidic chip to evaluate cells' morphological changes and proliferation when exposed to the EGF gradient. They found that when cells are cultured with CAFs, their invasive behavior increases [11]. In another study, Xiaohui et al designed a microfluidic droplet chip to study the angiogenesis of HUVEC cells. This system allows the secretion of VEGF, which stimulates angiogenesis. They found that the process of angiogenesis was stopped in the presence of the anticancer drug Fingolimod [10]. Also, Kong et al. designed a microfluidic system to measure the potential of different types of lung cancer cells for metastasis. The results showed that the potential for metastasis in lung, bone marrow, and liver cells was far greater than muscle cells. [7,8].

Conclusion: Recent developments show that microfluidic chips are a suitable platform for evaluating cancer cells' invasive behavior, affecting the treatment and effectiveness of drugs and leading to the death of patients.

Keywords: microfluidic chips, 3D cell culture, spheroid, cancer, invasive behavior.

Microneedle drug delivery system with different drug concentration (Research Paper)

Hajar Moghadas,[1,*]

1. Department of mechanical engineering, Gas and Petroleum Faculty, Yasouj University, 75918-74831, Iran

Introduction: Microneedles are new tools for transdermal drug delivery [1]. They are local drug administration. Because of their small dimension, microneedle can't reach the nerve so they are the pain-free devices that make them more popular than the other kind of drug delivery systems [2]. Different parameters affect the microneedles' drug delivery efficiency, including microneedle shape and material, the loaded drug, and the skin properties [3]. Experimental and numerical investigations can evaluate the effect of each parameter and show the order of their importance [4]. Simulation and numerical analysis are helpful and cost-effective approaches to study the effect of different parameters on the drug delivery ability of the microneedles [5]. In this work, diffusion of the meloxicam (as the sample drug, meloxicam is pain mitigation that is used for some animals like dogs and cats [6]) into the cattle skin is stimulated by the aid of COMSOL software. The effect of the time and drug concentration in the diffusion pattern through the skin is evaluated for a tapered shape microneedle with 250 µm base diameter and 500 µm height.

Methods: To simulated drug diffusion from a microneedle in to the skin, COMSOL Multiphasic 5.6 is used. The computational domain is a large rectangular geometry as a piece of skin in which a tapered microneedle is inserted. The microneedle has a 250 µm base diameter and a 500 µm height. The deep of the rectangular domain is chosen 4000 µm and the length of the domain is chosen 5000 µm means 10 times the microneedle base diameter to ensure providing edge effect in the result. The governing equation of the diffusion is applied as bellow: $(dc_i)/dt+ \nabla \cdot J_{(i)}= R_i$. (1) And Fick's first law: $J_{(i)}=-D_i \nabla c_i$ (2) Where c_i is the drug concentration [mol/m3], t is time [s], $J_{(i)}$is the flux, Ri [mol/(m3.s)] is the mass source of ci, Di is the diffusion coefficient [m2/s] and ∇ is the gradient operator. The boundary conditions of the computational domain are set as c(0)= 0 for all points in the skin and c(0)= 1·43×〖10〗^(-4) [mol/m3] for microneedle. Diffusion coefficient of meloxicam is set as D=1·5×〖10〗^(-9) [m2/s], [6]. The drug diffusion is simulated using Transport of Diluted Species under a time-dependent model for different initial drug concentrations at different time periods.

Results: The simulation of the drug diffusion through the cattle skin is shown in figure 1 for initial drug concentration c(0)= 1·43×〖10〗^(-4) [mol/m3] and

c(0)= 2·86×〖10〗^(-4) [mol/m3] at different time, t=100 s, t=500 s and t=1000 s. After microneedle insertion, the drug will diffuse through the skin. The contours of concentration demonstrate the diffusion pattern by passing time. As illustrated the diffused domain has a circular shape because the skin property is supposed to be isentropic. By increases the time drug diffuse to more region. For higher initial concentration the diffused domain becomes larger at the given time. The obtained simulation results provide valuable data about the effect of microneedle drug concentration on the drug diffusion into the skin.

Conclusion: Drug delivery into the skin via a microneedle is simulated at different drug concentrations. The obtained results have valuable data about the drug diffused domain in the skin and the time of the drug insertion. Increasing the time of insertion or initial drug concentration increases the penetration depth of the drug. Microneedles are new pain-free transdermal drug delivery devices and promising powerful tools for modern adjustable and released controllable drug delivery systems into the other organs.

Keywords: Microneedle, Drug delivery, Simulation, Concentration

MicroRNA-138-5p modulates cell proliferation and sensitivity to Taxol in bladder cancer cells (Research Paper)

Mahtab Kadkhodayi,[1] Reza Safaralizadeh,[2,*] Behzad Baradaran,[3] Vahid Asghariazar ,[4] Mohammad Amin Doustvandi,[5]

1. Department of Animal Biology, Faculty of Natural Sciences, The University of Tabriz, Tabriz, Iran
2. Department of Animal Biology, Faculty of Natural Sciences, The University of Tabriz, Tabriz, Iran
3. Immunology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
4. Immunology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
5. Immunology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Introduction: Bladder cancer (BC) is one of the most common malignancies worldwide. Chemotherapy based on Taxol is the standard treatment for a range of cancers, including BC, but chemoresistance is mainly responsible for relapses of bladder cancer during clinical therapy. MicroRNAs (miRs) have been demonstrated to promise as a therapeutic factor in combination therapy of BC. Downregulation of miR-138-5p is reported in human bladder cancer. We aim to investigate the association of miR-138-5p expression with the sensitivity of bladder cancer EJ138 cells to Taxol.

Methods: EJ138 cells were transfected with miR-138-5p mimics and treated with Taxol in a combined manner or separately. The efficacy of transfection was verified by qRT-PCR. The half-maximal inhibitory concentration (IC50) value of Taxol in EJ138 cells and the effect of miR-138-5p on cell proliferation and chemosensitivity to Taxol were measured using the MTT assay.

Results: These data verified the tumor-suppressive role of miR-138-5p in BC cells. Furthermore, the results showed that the miR-138-5p+Taxol combination group showed lower cell viability rates than that of the miR-138-5p transfected group or Taxol treated group alone. The IC50 of Taxol and miR-138-5p+Taxol in EJ138 cells were 0.735 µg/ml and 0.09125 µg/ml, respectively. This might indicate that miR-138-5p could decrease the efficient dose of Taxol and might be effective in reducing Taxol-related potential side effects in bladder cancer patients.

Conclusion: Upregulation of miR-138-5p suppresses EJ138 cell proliferation and increases the sensitivity of these cells to Taxol. Consequently, the

combination of miR-138-5p with Taxol would provide a potential strategy to be considered as a treatment option against bladder cancer.

Keywords: Bladder cancer; miR-138-5p; Taxol,; Chemosensitivity; EJ138 cells

MiR-340-5p involved in Trastuzumab Resistance in Breast Cancer through upregulating MET (Research Paper)

Farzaneh Karimi,[1] Ahmad Ghafarpour ,[2] Kazem Dastjerdi ,[3,*]

1. Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran
2. Department of Medical Biotechnology, Faculty of Medicine, Birjand University of Medical Sciences, Birjand, Iran.
3. Department of Medical Biotechnology, Faculty of Medicine, Birjand University of Medical Sciences, Birjand, Iran

Introduction: Introduction: Breast cancer is the most frequent leading cause of cancer-related mortality among females worldwide. Although trastuzumab provides pivotal clinical benefits for human epidermal growth factor receptor-2 (HER2) positive breast cancer patients, its efficacy is often limited by the emergence of chemoresistance. Accumulating evidence has demonstrated that microRNAs significantly contribute to anti-cancer drug resistance. The purpose of the current study was to evaluate the role of miR-340-5p in trastuzumab resistance in HER2-positive breast cancer cell lines using the bioinformatics approaches to propose suitable therapeutic methods to overcome trastuzumab resistance.

Methods: Materials and Methods: Potential target genes were detected using TargetScan and miRDB databases. STRING website and Cytoscape software were also used for investigating gene-gene interactions. Moreover, to provide the generated modules of the selected genes Gephi software was used. Eventually, we investigate the target gene expression in trastuzumab-resistant and trastuzumab-sensitive breast cancer cell lines using PCR.

Results: Results: Our findings revealed that the downregulation of miR-340-5p in breast cancer trastuzumab-resistant cell line can upregulate MET in comparison to trastuzumab-sensitive cell line.

Conclusion: Conclusions: To sum up, the current study reported that upregulation of miR-340-5p or downregulation of its target gene MET can reverse trastuzumab resistance in breast cancer. Therefore, this method might be a novel strategy to overcome trastuzumab resistance in HER2-positive breast cancer.

Keywords: MiR-340-5p, MET, Trastuzumab Resistance, Breast Cancer

miR-492: A novel potential therapeutic target an prognostic factor in cancers (Review)

Anita Alizadeh,[1,*]

1. M.SC. student of Genetics, Department of Biology, Higher Education Institute of Rab-Rashid, Tabriz, Iran

Introduction: microRNAs (miRNAs) are a class of small non coding RNAs with approximately 22 nucleotides in length and have ability to regulate gene expression in post transcriptional level. miRNAs as highly conserved non coding RNAs have crucial functions in different biological processes of human cancers. Moreover, they can be regulated by circular RNAs (circRNAs). Furthermore, stability of miRNAs in body fluids and their tumor specific expression have introduced them as valuable candidates for early detection and effective treatments of cancer. miR-492 which is located at chromosomal position 12q22 which has been demonstrated to be dysregulated in various types of human cancers.

Methods: The present study was conducted in a review of the digital and library resources also authentic scientific sources of the PubMed site and google scholar with the key word of mir-492 in cancer with aim to study interactions between miR-492 and other target genes and signaling pathways which involved in tumorigenesis of cancer.

Results: Studies have shown that miR-492 is upregulated in various types of cancer such as gastric, prostate, ovarian, breast, bladder, cervical, colon, endometrial, hepatoblastoma and retinoblastoma. miR-492 acts as an oncogene in these cancers and plays an important role in tumorigenesis by affecting cell proliferation, invasion, migration, epithelial to mesenchymal transition (EMT) and apoptosis which exerts these regulatory effects by interfering with various circRNAs such as circTET1 and circ-0001368 and signaling pathways including wnt/βcatenin and PI3K/AKT, PTEN pathways.

Conclusion: Given that, this review summarizes the related research of miR-492 as the multifunctional miRNA in various cancer development and tumorigenesis. Accordingly, miR-492 may acts as a novel potential biomarker for cancer diagnosis or treatment in future.

Keywords: miRNAs, miR-492, cancer, biomarker, tumorigenesis.

miRNA/lncRNA axis of a ceRNA network promotes the development of FL cancer by regulating Wnt signaling pathway: an integrated bioinformatics and systems biology analysis (Research Paper)

Arian Sadeghi,[1] Mohammad Rezaei ,[2] Mansoureh Azadeh,[3,*]

1. Zist Fanavari Novin Biotechnology Institute
2. Zist Fanavari Novin Biotechnology Institute
3. Zist Fanavari Novin Biotechnology Institute

Introduction: Follicular lymphoma (FL) is the second most frequent non-Hodgkin lymphoma accounting for about 10-20% of all lymphomas in western countries. The median age at diagnosis is 60 years old and there is a slight predominance in women . Bone marrow involvement is present in more than 50% of patients. The disease is usually characterized by an indolent clinical course response to initial therapy with frequent relapses and shorter duration responses to salvage therapy.

Methods: To start, NCBI Gene Expression Omnibus (GEO) has been chosen to get the Proper GSE, A related gene expression profile has been downloaded and analyzed by Rstudio in order to find the genes which have notable up and down expression regulations, that by analysis of candidate genes' pathways, HAPLN1, SFRP2, and SFRP4 has been selected. Moreover, miRWalk and miRTarBase databases have been used to identify numerous target microRNAs of selected genes. Eventually, by analyzing pathways involved in FL, the required microRNA has been selected. By examination of related lncRNAs, since MALAT-1 lncRNA had the most reliance and specificity, it has been selected as another axis of our ceRNA network.

Results: Based on GEO analysis the desired GSE named GSE152068 was indicated among human stromal cells isolated from Follicular lymphoma (FL) or non-malignant reactive (RLN) lymph nodes. These analysis outcomes assigned that the GSE152068 was surprisingly enriched in several biological mechanisms. A total number of 12 up-regulated and 8 down-regulated genes from the GSE was indicated which by the Enrichr database the pathways of each were examined separately. Up-regulated genes pointed to related pathways named, Wnt signaling pathway and Interleukin-1 regulation of extracellular matrix that HAPLN1, SFRP2, and SFRP4 demonstrated a notable gene of these pathways.

Conclusion: According to the all mentioned events, concluded that hsa-let-7a-5p via overexpression of the HAPLN1 gene's function acts as a tumor growth factor in the Wnt signaling pathway of FL and AML. Thus, these

findings could provide promising comorbidity between these two types of cancer and their effect on each other. It also can lead us to a common method for the treatment of FL and AML patients.

Keywords: Follicular lymphoma- Systems biology - MALAT1- ceRNA network-HAPLN1

Modification of genetic alterations effects on brain tumor risk: substantial role of dietary factors (Review)

Fatemeh Vaghefi,[1] Fatemeh Karami,[2,*] SayedAlireza Mousavi,[3]

1. Department of Biology, School of Basic Science, Science and Research Branch, Islamic Azad University, Tehran, Islamic Republic of Iran
2. Department of Medical Genetics, Applied Biophotonics Research Center, Science and Research Branch, Islamic Azad University, Tehran, Islamic Republic of Iran
3. Department of Biology, School of Basic Science, Science and Research Branch, Islamic Azad University, Tehran, Islamic Republic of Iran

Introduction: Brain tumors usually arise in familial cancer predisposition syndromes or tend to be clustered in families. Owing to the role of lifestyle modulation on decreasing the chance of disabling the remained wild alleles, preventive personalized diet have been recently studied in various types of cancer as well as brain tumor. Present study was aimed to review the dietary factors that may change the risk in high risk individuals.

Methods: We explored the internet in Google Scholar, Pubmed, Pubmed Central and Bing search engines using main key words including Breast cancer risk, gene polymorphism, gene expression, variant and dietary factors. All the manuscripts after 2000 were included in the present review.

Results: Among different dietary factors, it was found that polyunsaturated fatty acids (PUFA) can change the risk of brain tumors through affecting the expression of mTOR, immunocompromising and inflammatory cytokines, cell cycle and proapoptotic genes.

Conclusion: Owing to the contradictory results on different parts and types of diet on modulation of brain tumor pathogenesis, further studies are warranted to determine the exact quantity of different foods, vegentables and even supplements on either prevention or treatment of brain tumors.

Keywords: Brain tumor, dietary factor, risk, gene alteration

Molecular biocellular cancer with emphasis on the role of biomarkers in cancer diagnosis (Review)

Fateme Eshaghi,[1,*] Fateme Ejtehadi,[2] Bahar Khousian,[3]

1.
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Introduction: The term "cancer" refers to more than 277 types of cancer, a process in which normal cells gradually turn into malignancies. . This damage can be the result of endogenous processes such as DNA replication errors, the inherent chemical instability of some DNA bases, or the attack of free radicals generated during metabolism. DNA damage can also be caused by interactions with exogenous factors such as ionizing radiation, ultraviolet radiation, and chemical carcinogens. 99.9% of genes are the same in all humans, and only 0.1% of human genes are different, which causes It becomes the apparent diversity of human beings. About 93% of cancers are the result of environmental factors and only 7% of them are hereditary. There are more than one hundred thousand types of chemicals in our environment, of which only 35,000 have been analyzed and about 300 of them produce cancer. 65,000 chemicals left in nature have not yet been tested. Cancer results from uncontrolled cell division that results from environmental factors and genetic disorders. The four groups of genes that frequently become abnormal play an important role in the production of cancer cells:- 1Oncogenes, the proliferation of their activity causes the uncontrollable growth of cells 2-tumor inhibitory genes 3-DNA repair genes 4-apoptotic genes The development of biology has led to a better understanding of these genes: oncogenes, are basically activated by structural or regulatory changes which lead the cell to continuous multiplication.Tumor suppressor genes, which can inhibit illegally activated cell cycle. They help tumor growth by creating missing mutations or permanent shrinkage, for example. With methylation; Apoptosis inhibitor genes that can contribute to tumor development by raising the threshold for apoptosis, and genes that cause apoptosis that can help by killing or inactivating apoptotic tumor cells. DNA repair genes that are inactivated can counteract the natural deletion of cells that carry potential cancer mutations. Hereditary mutations in DNA repair genes can lead to familial cancer syndromes. Chemicals cause cancer cells to form called carcinogens. Cigarette smoke contains about 40 carcinogenic chemicals that often produce lung cancer. There are more than 100,000 types of chemicals in nature that directly or indirectly affect the cytoplasm and cell nucleus, leading to genetic disorders that eventually lead to mutations. Viruses and bacteria and Different rays, in turn, produce hereditary cancers, which account for about 7% of all cancers.Cancerous tissues are divided into 6 groups: blood, lymph nodes, sarcoma, carcinoma, embryonic cells, sex

cells. Cancer is a disease that disrupts intercellular relationships and disrupts vital and key genes. These molecular irregularities affect the cell division cycle and lead to non-differentiation of cells. Biomarkers are molecules that indicate a normal or abnormal process in your body.one of the important tasks of biomarkers is identification of progression and stage of cancer. so that appropriate treatment can be provided to the patient at that particular stage. miRNAs can be good biomarkers for detection and even appropriate treatment for cancer in the near future. The expression levels of some of them (miR-373 and miR-335, miR-126, miR-31, miR-21, miR10-b(are altered in cancer, which could codify the diagnostic application of another class of non-large RNAs. LincRNA, noncoding intervening RNAs are also recognized as accepted biomarkers in breast cancer metastasis, including the use of miRNAs, which can be referred to as HOTAIRs. Also array lncRNAs can have high diagnostic value. Other biomarkers you can count on are cell free Nucleic Acid (cfNA) These are mRNAs, DNAs and microRNAs that can be detected in the blood of cancer patients that tumor cells are secreted.The sequencing of these nucleic acids can also identify the various polymorphisms and mutations identified. The use of secretory nucleic acids in tumors has several benefits. It is possible to study the blood of cancer patients at certain intervals , and even to study genetic changes , cancer. These changes include natural changes in cancer cells, and changes that occur as a result of treatment. Another biomarker is the marker of gene expression. Obviously, the order in normal cells changes in gene expression in cancer cells. Finally Recognition of important genes involved in cancer in recent studies can show promising prospects for the diagnosis and treatment of cancer.

Methods: Review of scientific articles and journals

Results: Cancer is a disease that results from damage to DNA, which can be the result of endogenous processes or exogenous factors. In other words, the effects of environmental factors and genetic disorders can cause cancer. Only 7% of cancers are hereditary and 93% are the result of environmental factors. Four groups of genes (1. Oncogenes 2. Tumor inhibitory genes 3. DNA repair genes 4. Apoptotic genes) play an important role in cancer cell production. There are more than one hundred thousand types of chemicals in our environment and about 300 Some of them produce cancer. 65,000 chemicals left in nature have not yet been tested. Chemicals cause cancer cells to form called carcinogens. Viruses, bacteria, and various rays, in turn, produce inherited cancers. Biomarkers are molecules that indicate a normal or abnormal process in your body and may be a sign of a condition or disease. Tumor markers (cancer biomarkers) are markers that are the result of secretion from a tumor cell or the result of necrosis and apoptosis of these cells. Specific changes in cancer cell molecules can be considered as biomarkers if they can be measured. Biomarkers can be RNA, DNA, proteins and metabolites.

Conclusion: nowdays, deployment of molecular biology with the knowledge of genes and biomarkers, etc., has led to early detection of cancer and help in treatment and even prevention. Because a change in genes is the first stage of cell cancer, the identification of molecular biomarkers is very important in the early detection of this progressive disease. Also today, gene therapy is considered as one of the new methods of treating many genetic and complex diseases such as cancer. In recent decades, the use of non-invasive RNAs, including microRNA, in the diagnosis and treatment of cancer has attracted the attention of many researchers around the world. Various studies have shown that increasing or decreasing the level of microRNA expression in various carcinogenic processes and therefore modifying these changes can be effective in treating cancer.

Keywords: biology/gene/cancer/biomarker

Molecular Characterization of Staphylococcus aureus Isolated from Clinical Samples Based on 16srRNA, rpoB, and hsp70 Genes by MLSA (Research Paper)

Hoseiny Khorram Abadi Elham,[1,*] Zaker Bostan Abad saeed,[2]

1.
2. Department of biotechnology,School of Basic Sciences,Parand Branch,Islamic Azad University,Tehran,Iran

Introduction: Staphylococcus aureus is a commensal Gram-positive organism present on the skin and mucosal surface with the capability of surviving on dry surfaces due to its thick peptidoglycan layer [1]. Risk factors of S. aureus infections include external devices, history of surgery, and extensive antibiotic use [2]. Patients at risk of S. aureus infections include neonates, children with poor sanitation, women during menstruation, and patients with intravascular catheters. This microorganism could mainly lead to the bacteremia, endocarditis, osteomyelitis, pneumonia, skin and soft tissue infections [3]. Although S. aureus is generally considered as an opportunistic pathogen, some clones may be more capable of causing invasive disease due to the presence of certain virulence factors facilitating access to normally sterile sites [4]. Recently, S. aureus has exhibited great resistance against multiple antimicrobial agents, which is of great concern. Methicillin-resistant S. aureus (MRSA) strains; including hospital-acquired MRSA (HA-MRSA), community-acquired MRSA (CA-MRSA), and livestock-associated MRSA (LA-MRSA) strains; are resistant to all β-lactam antibiotics through acquiring mobile genetic elements called staphylococcal cassette chromosome mec (SCCmec) [5-7]. In addition to acquiring antibacterial resistance, differences in staphylococcal pathogenicity, depending on different geographical regions and epigenetics, necessitate the investigation of the genomic structure, polymorphism, and phylogenetic relationships between different S. aureus clinical isolates. ..references?Multi-locus sequence analysis (MLSA) is a powerful high-resolution method which provides data on genetic changes in housekeeping genes and could be served as a valid technique for the study of epidemiological relationships [8]. In fact, MLSA is able to compare the primary DNA sequences of multiple conserved protein-coding loci in order to assess the diversity and relationship between different isolates and to determine the sources and evolutionary alterations of different taxa. Objectives: This study aimed to investigate the genetic diversity of S. aureus clinical strains isolated from different body sites. In this study, a MLSA protocol was developed based on genes coding for β-subunit bacterial RNA polymerase (rpoB) and heat-shock protein 70 (hsp70) as well as 16S rRNA gene. These genes are essential for bacteria, and their polymorphism is highly important in determining bacterial genetic behaviors corresponding to different environmental factors

Methods: growth conditions&Isolation of Genomic DNA&Polymerase Chain Reaction (PCR) and Sequence data analyses&Sequencing&Findings Genetic variations by MLSA&Phylogenetic analysis of the strains using the Neighbor Joining method andPhylogenetic analysis of the strains using the Maximum Parsimony method.

Results: Phylogenetic trees constructed based on 16s rRNA gene using the neighbor joining method showed that the Strain 14 was different from the Strains 23, 49, and 42 (>99% difference) as well as the Strains 5 and 6 (>73%). Moreover, Strain 48 showed a sequence different from the Strains 6, 14, 15, 19, 22, 23, 42, and 49 (>99% difference). Finally, the Strain 50 was different in sequence from the Strains 1, 2, 3, 4, 5, 6, 11, 16, 20, 25, 30, 33, 37, 38, 39, 40, 46, 48, and 49 (Fig. S1A). Phylogenetic trees based on hsp70 gene showed that the Strains 5, 30, 43, and 49 were different from other strains in sequence (>99% difference). However, other strains were highly correlated, and the sequence similarity of the strains could be considered as an indicative of common ancestors (Fig. S2A). Based on the rpoB gene sequences, the Strain 11 showed a high correlation to the reference strain and Strains 2, 3, 5, 11, 24, 26, 37, 39, and 43, while it was different from other strains (>99% difference). Moreover, the Strain 15 was highly correlated with other strains, except for 19, 25, 29, 35, 41, 45, and 49 (>99% difference). Phylogenetic trees constructed based on the concatenation of 16s rRNA, rpoB, and hsp70 genes sequences by maximum parsimony and neighbor-joining methods showed that the Strain 5 was different from the Strains 6, 15, 19, 30, 32, 42, 46, 47, 48, and 40 with a bootstrap value of 99%. Moreover, the Strain 11 showed a phylogenetic difference with the Strains 1, 2, 3, 4, 5, 6, 15, 19, 30, 32, 42, 46, 47, 48, and 49 with a bootstrap value of 99%. However, other strains were highly similar in sequence and showed a close relationship to one other. Notably, the Strain 24 only showed similar genetic sequence to the reference strain and Strain 7 and showed 99% difference with other strains (Fig. S4A). According to the results of phylogenetic analysis based on 16s rRNA gene using maximum parsimony method, all S. aureus isolates showed similar genetic sequences and were not phylogenetically different and were presented in a monophyletic manner. However, it must be noted that the Strains 13 and 39 showed a trivial difference with other isolates with a bootstrap value of 63% (Fig. S1B). Molecular analysis based on hsp70 gene indicated that the Strains 2, 5, 27, and 30 were different from other strains with a bootstrap value of 62%, while the Strains 1 and 24 were different from other strains with a bootstrap value of 61% (Fig. 12B). Finally, Phylogenetic analysis based on rpoB gene using the maximum parsimony method revealed the differentiation of the Strains 5 and 11 with 99% bootstrap value as well as the differentiation of the Strain 33 with 53% bootstrap value compared to the other strains (Fig. S3B). Phylogenetic analysis based on 16srRNA, rpoB, and hsp70 genes in concatenation indicated that the Strains 5 and 11, 1 and 24,

and 37 and 43 were different from other strains with the respective bootstrap values of 99, 58, and 51%.

Conclusion: today, understanding the phylogeny of bacteria based on housekeeping genes is of great importance. In this study, the polymorphisms were determined, and a MLSA technique was developed for 50 S. aureus clinical isolates based on 16S rRNA, hsp70, and rpoB genes. The MLSA method was clearly capable of discriminating between the S. aureus genotypes. Overall, there was a high genetic diversity in the three studied MLSA loci among the 50 S. aureus clinical isolates compared to the reference strain of S. aureus NCTC 8325. The use of multi-locus sequence analysis and the study of polymorphisms in S. aureus clinical isolates are proposed for infection control and surveillance.

Keywords: Staphylococcus aureus, Polymorphism, Multi-locus sequence analysis (MLSA).

Molecular Detecion of Chlamydia trachomatis, Ureaplasma urealyticum, Mycoplasma hominis and Listeria monocytogenes in Women with Recurrent Miscarriage using PCR method (Research Paper)

Maryam Tohidpour,[1,*] Mohammad Hassan Shahhosseiny,[2] Sedigheh Mehrabian,[3] AboTaleb Saremi ,[4]

1. Department of Microbiology, College of Biological Sciences, North Tehran Branch, Islamic Azad University, Tehran, Iran
2. Department of Microbiology, College of Basic Sciences, Shahr- e-Qods Branch, Islamic Azad University, Tehran, Iran
3. Department of Microbiology, College of Biological Sciences, North Tehran Branch, Islamic Azad University, Tehran, Iran
4. MD, Gynecologist, Subspecialty of Infertility, IVF and Laparoscopic surgery, Sarem Fertility and Infertility Research Center (SAFIR), Sarem Cell Research Center(SCRC), Sarem Women's Hospital , Tehran/ Iran

Introduction: In recent years, recurrent abortion, as a major medical problem, has attracted the attention of many researchers and it is considered as a big challenge with serious psychological problems and stressful experiences for couples. Recurrent abortion is a complex multifactorial phenomenon triggered by a variety of factors, including genetic, hormonal, and immunological problems, as well as uterus structural abnormalities, infections during pregnancy, etc. Among the mentioned predisposing factors, infections, due to negative impacts on reproductive function, can lead to failure in fertilization, so they should be timely screened, diagnosed, and treated with antibiotics. Due to the importance of this issue, current study aimed to detect Chlamydia trachomatis, Ureaplasma urealyticum, Mycoplasma hominis, and Listeria monocytogenes in women with recurrent miscarriage using PCR method.

Methods: In this study, a sterile swab was used for sampling from the endocervix. The participants included 100 women with a history of recurrent miscarriage referred to infertility & prenatal clinic of the Sarem Women's Hospital. The samples were used for performing vaginal culture and PCR that was conducted after DNA extraction by the phenol-chloroform method to identify C. trachomatis, U. urealyticum, M. hominis, and L. monocytogenes.

Results: Out of 100 samples, 14% were positive for C. trachomatis, 11% were positive for U. urealyticum, 4% were positive for M. hominis, 3% were positive for L. monocytogenes, and 2% were positive for co-infection. In the vaginal culture test, all the samples showed a WBC count above the normal range and the presence of bacteria. Based on the results of PCR test, a relatively high prevalence was observed in relation to C. trachomatis, U.urealyticum, M. hominis and L.monocytogenes in women with a history of 3

miscarriages compared to women with a history of more than 3 miscarriages. However, the prevalence of this group of bacteria had no significant association with age and number of abortions in women with recurrent miscarriages (P>0.05).

Conclusion: According to the results of this study, it is recommended to screen pregnant women, especially those undergoing assisted reproductive techniques (ART), for these bacteria to prevent infection-induced recurrent miscarriages. Polymerase Chain Reaction (PCR), as a highly sensitive and accurate molecular method, is suggested to be incorporated in the country's pregnancy health care programs to identify these bacteria and maintain pregnant women's health. Finally, timely antibiotic therapy can be effective in reducing the incidence of recurrent abortions among women.

Keywords: C.trachomatis, Uurealyticum, M.hominis, L.moncytogenes, Recurrent Miscarrige

Molecular Determination of Frequency of Human Papillomavirus Infection and it's genotypes among Patients with Esophageal Cancer in Bushehr Province, 2009-2019 (Research Paper)

Reza Taherkhani,[1] Fatemeh Farshadpour,[2,*]

1. Department of Virology, School of Medicine, Bushehr University of Medical Sciences
2. Department of Virology, School of Medicine, Bushehr University of Medical Sciences

Introduction: Esophageal cancer is the eighth malignant tumor and the sixth cause of cancer deaths in the world. The role of infectious agents and oncoviruses such as human papillomaviruses in contaminating esophageal, which can occur by oral transmission or through blood or lymph, is mentioned as a potential risk factor for esophageal cancer. This study was conducted to determine the prevalence and genotype distribution of human papillomavirus in paraffin-embedded tissue specimens from patients with esophageal cancer in a 10-year period in Bushehr province using nested-PCR technique.

Methods: This study is a descriptive cross-sectional study. The study population includes paraffin-embedded specimens of patients with esophageal cancer referred to the Shohadaie Khalij-Fars Hospital in Bushehr during 2009 to 2019. Paraffin-embedded tissue specimens from 44 patients with esophageal cancer, as well as 103 paraffin-embedded tissue samples with benign lesions of esophagus (inflammatory, hyperplasia, polyp specimens) as control group were investigated for nested PCR. Data were analyzed using SPSS software, Chi-square and Fisher's statistical tests.

Results: The mean age of 44 patients with esophageal cancer, which were investigated in molecular analysis, is 69.77 ± 14.52 (range from 35 to 94 years). Most of the patients are age 80 and older, and then in the age range of 70 to 79 years. There were 29 men with a mean age of 67.24 ± 16.13 and 15 women with a mean age of 74.66 ± 9.43. The prevalence of esophageal cancer in men is higher than that of women, and the mean age in women is higher than that of men, but the difference in mean was not statistically significant. Most cases of esophageal cancer were from 2014 to 2019. In men, the most common type of esophageal carcinoma was adenocarcinoma (69%) and in women, the most common type of esophageal carcinoma was squamous cell carcinoma (80%). The mean age in patients with squamous cell carcinoma was higher than that in adenocarcinoma, but the mean differences were not statistically significant. The prevalence of HPV infection in 44 samples of esophageal cancer was 9.1% (4 cases) and in 103 samples with benign lesions of esophagus (control group) was 1.9% (2 cases). In the case group, the prevalence of HPV infection in women was almost twice as

high as that of men, and the mean age in individuals with HPV infection was higher than those without HPV infection. Most of the cases with esophageal cancer, which were positive for HPV infection, are squamous cell carcinoma. Overall, there was no significant statistically relationship between gender, age, city, year and type of malignant lesions of esophagus with the prevalence of HPV infection (p value> 0.05).

Conclusion: The overall prevalence of HPV infection in patients with esophageal cancer was 4.7 times the prevalence of HPV infection in non-cancer patients, although this increase was not statistically significant. However, the use of the human papillomavirus vaccine in some patients with benign lesions of esophagus may be effective in preventing the progression of these lesions to the malignancy. It is also suggested that, in addition to HPV, the role of other risk factors for esophageal cancer such as tobacco use, alcoholic beverages, dietary deficiencies and diet, as well as the role of other infectious agents will also be investigated.

Keywords: Human Papillomavirus, Esophageal cancer, Bushehr province, nested-PCR method

Molecular Dynamic Simulation and Docking of Cyclophilin A Mutants with its Potential Inhibitors (Research Paper)

Alireza Mohebbi,[1,*] Reyhane Shaddel,[2] Saman Saeidi,[3]

1. Department of microbiology, school of medicine, golestan university of medical sciences, Gorgan, Iran
2. Student Research Committee, School of Medicine, Golestan university of medical sciences, Gorgan, Iran
3. Student Research Committee, School of Medicine, Golestan university of medical sciences, Gorgan, Iran

Introduction: Cyclophilin A (CypA) is involved in various human biological processes. Its role in many pathological conditions makes it a promising target for treating human diseases, such as viral infections. The aim of the present study was to investigate docking of CypA mutants with its potential inhibitors using molecular dynamic simulation ((MDS).

Methods: The crystallographic structure of CypA was extracted from the protein database (PDB). Important CypA substitutions were obtained from the literature. CypA inhibitors were taken from chemical databases. The affinity and binding sites of the compounds to CypA and its mutants were also scaled through Autodock Vina. Root-mean-square deviation (RMSD), radios gyration, Lenard-jones potential, and hydrogen bonding were investigated by using MDS for 600 ps.

Results: The findings revealed that SangfA and HBF-0259 had more affinity to the CypA (-7.8Kcal/mol and -7.5Kcal/mol, respectively). Conformational changes were observed in CypA W121A/F mutants. SangfA complexed with CypA and its mutants had relatively stable RMSD. Higher Lenard-Jones potential has been observed in the interaction of SangfA to W121A, HBF-0259 to M61, and SCY-635 to H70F. The SangfA had a higher HBs ratio with CypA.

Conclusion: Given the higher affinity of SangfA and HBF-0259 to CypA and its mutants, they would influence the stability of the protein. RMSD analysis revealed that SangfA is probably ligated to CypA and its mutants, which are relatively stable. Substitution at W121 residue would reduce inhibitor binding to CypA.

Keywords: HBF-0259, Cyclophilin A, Sanglifehrin A, CypA inhibitors, Molecular Dynamic Simulation

Molecular genetics in Radicular cyst (Research Paper)

Hamideh Kadeh,[1] Shirin Saravani,[2,*]

1. Oral & Dental Disease Research Center, Department of Oral & Maxillofacial Pathology, School of Dentistry, Zahedan University of Medical Science, Zahedan, Iran
2. Oral & Dental Disease Research Center, Department of Oral & Maxillofacial Pathology, School of Dentistry, Zahedan University of Medical Science, Zahedan, Iran

Introduction: Cysts are lesions that are more common in the oral cavity than in other parts of the body. Radicular cysts are the most frequently odontogenic cysts that are discovered in the apical region of a necrotic tooth. Recent findings about events at the molecular level, combined with the clinical behavior of lesions, provide better insight into the nature of lesions. This study explain gene expression profiles and others genetic variation of radicular cysts in order to uncover possible mechanism of pathogenesis that would help in the diagnosis and discovery of novel therapeutic options.

Methods: Using the main keywords of "Radicular cyst", "gene expression"and "molecular genetics" a comprehensive research was performed among several research databases.

Results: Regarding bone metabolism, receptor activator of nuclear factor-B ligand (RANKL) gene has been extensively examined because of its important role in bone resorption around the tooth apex. This gene is part of the pathway that activates osteoclasts and is inhibited by osteoprotegerin. It has been reported that the RB1, TP53, XIAP, CASP3 and CASP9 genes may be important in the development and increased cell proliferation of odontogenic cysts, including radicular cysts. Loss of heterozygosity of FHIT is observed in 10% of radicular cysts cases while LOH of P53 gene is not observed in radicular cysts. In another study, the importance of MMP1, MMP2, TIMP1, TIMP2 genes expression in the pathogenesis of periapical inflammatory lesions was reported. Also it has been reported that the FOXP3 gene promotor methylation was correlated with FOXP3 transcript levels inversely, and this shows that FOXP3 may be important in periapical lesion development.

Conclusion: Detection of Gene expression profiles and others genetic variation of odontogenic cysts, including radicular cysts is critical in order to uncover possible mechanism of pathogenesis that would help in the diagnosis and discovery of novel therapeutic options for these lesions.

Keywords: Radicular cyst, gene expression, RANKL, P53, MMP

Molecular Identification and Isolation of Novel Uricase-Positive Bacteria from Soil Enriched with Poultry Manure (Research Paper)

Parisa Pakbaz,[1] Nematollah Razmi,[2] Nima Bahador,[3] Safoura Sameni,[4,*]

1. Department of Biochemistry, Shiraz Branch, Islamic Azad University, Shiraz, Iran
2. Department of Biochemistry, Shiraz Branch, Islamic Azad University, Shiraz, Iran
3. Department of Microbiology, Shiraz Branch, Islamic Azad University, Shiraz, Iran
4. Department of Biochemistry, Shiraz Branch, Islamic Azad University, Shiraz, Iran

Introduction: Soils, especially agricultural soils contain a collection of minerals, organic matter, and beneficial microorganisms. Soil microorganisms, including bacteria, are capable of biosynthesis and secretion of many enzymes, which can decompose biomolecules of the surrounding sewage and fertilizers. Microbial activity will improve the volatilization of ammonia from poultry manure, denoting that uric acid, as the dominant non-protein nitrogenous compound form of this fertilizer, will be converted into allantoin by microbial uricase. This research aims to identify and isolate the uricase-producing bacteria from soil samples enriched with poultry manure from Shiraz, Iran.

Methods: In this study, 20 soil samples enriched with poultry manure from different parts of South East Shiraz, were diluted and the supernatants were analyzed for bacterial isolation. Later the bacteria were cultured in either minimal uric acid or uric acid-free medium. Uricase-positive bacteria, fed on uric acid as source of carbon and nitrogen. Different microbial and biochemical tests including gram stain, catalase, oxidase, nitrate reduction, sulfide, indole motility, hydrolysis of starch, and gelatin hydrolysis were performed. Lastly, uricase-producing bacterial strains were isolated through a PCR test.

Results: Twenty randomly selected soil samples were screened for microbial activity. Out of 9 bacterial species, 2 novel uricase-positive bacteria were isolated. Following the molecular examination, as confirmed by NCBI blast analysis, one strain was identified as Sphingobium sp. C1-1 and the other one was Bacillus flexus strain Til_Wak_24.

Conclusion: The results of this study validate the potential of poultry manure enriched soils in producing microbial uricase enzyme.

Keywords: Uricase positive bacteria, Minimal media, Uric Acid, Soil, Poultry Manure

Multiplex PCR for Detection of Genes for Staphylococcus aureus Enterotoxins from dairy products (Research Paper)

Mohammad Javad Forouzani-Moghaddam,[1,*]

1. Msc of Food Microbiology, School of Paramedical, Iran University of Medical Sciences, Tehran, Iran

Introduction: Staphylococcal food poisoning remains one of the three most common types of food poisoning in the United States; approximately 25% of all foodborne illnesses reported in the United States are caused by staphylococcal intoxication. Staphylococcus aureus is a ubiquitous bacterium, being both a human and a zoonotic commensal. As a result, S. aureus may be found in milk, other dairy products, vegetables, and raw and fermented meats. The bacterium is also highly salt tolerant, resistant to nitrites, and capable of growth in foods with a low water activity. S. aureus is regarded as potentially hazardous in foods due to production of heat-stable enterotoxins.Due to these characteristics, S. aureus is an important foodborne pathogen. At least nine enterotoxins (A, B, C, D, E, G, H, I, and J) may be produced by S. aureus.

Methods: Cultures were incubated statically overnight in tryptic soy brothat 37 °C. Following confirmation of PCR primer specificity, S. aureus ATCC 25923 were used in food inoculations. Conditions were optimized for multiplex PCR targeting both entC and nuc genes simultaneously in a single tube. Magnesium chloride, primer, and dimethylsulfoxide concentration titrations were conducted. Final reaction conditions included 2.5 ml of extracted DNA, 1 ml of dimethylsulfoxide, 2 ml of 25 mM magnesium chloride (Life Technologies), 20 pmol of forward primer, 20 pmol of reverse primer (for each gene), and 44 ml of PCR Supermix. The cycling profile was the same as described above, except the annealing temperature was increased to 56 °C.

Results: DNA was successfully extracted from as few as 10 CFU/ml S. aureus from skim milk or 10 CFU/20 g cheese. S. aureus possesses a thick peptidoglycan cell wall and is resistant to many techniques that easily lyse other cells. The application of lysostaphin was necessary for successful extraction of S. aureus DNA. They also noted that DNA yields from cheese were higher than DNA yields from skim milk, which were similar to results reported here. The reason for the higher yields of DNA from cheese may be due to the presence of naturally occurring cheese microflora.

Conclusion: The developed multiplex PCR for S. aureus allows detection and differentiation of S. aureus and can be completed in 6 h. The sensitivity of the assay is far higher than the 106 number of S. aureus cells required for

foodborne intoxication and the assay can be a useful tool for the food industry. This assay can be used by the dairy industry to monitor critical control points in a hazard analysis critical control point plan for detection of S. aureus either at milk receiving or to assess post processing product contamination.

Keywords: Multiplex PCR, Detection, Staphylococcus aureus, dairy products

nanofibrous mat loaded with growth factors, silver sulfadiazine and hair follicle bulge stem cells can facilate wound healing in rat (Research Paper)

fereshteh nejaddehbashi,[1,*] Eskandar moghimipour,[2] mahmoud orazizadeh,[3] vahid bayati,[4] mohammadreza abbaspour,[5] Mahmoud hashemitabar,[6]

1. Cellular and Molecular Research Center, Medical Basic Sciences Research Institute, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
2. Nanotechnology Research center, Faculty of Pharmacy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
3. Cellular and Molecular Research Center, Medical Basic Sciences Research Institute,Department of Anatomical Sciences, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
4. Cellular and Molecular Research Center, Medical Basic Sciences Research Institute,Department of Anatomical Sciences, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
5. Targeted Drug Delivery Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran
6. Cellular and Molecular Research Center, Medical Basic Sciences Research Institute,Department of Anatomical Sciences, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Introduction: Background: Despite special advances in regenerative medicine, wound healing is a challenging medical problem. The skin is the largest organ in the human body that has essential and important functions, so any damage to its normal structure should be treated as soon as possible. Easy access to skin stem cells has received a great deal of attention in its therapeutic applications. Cell therapy is a new method in restorative medicine, especially when old therapies have disappeared. Candidate populations for therapeutic applications include mesenchymal stem cells, hair follicle stem cells, and pluripotent cells. Hair follicle bulge stem cells with scaffold and growth factors can improve wound healing.

Methods: Materials and methods: In this study PCL/SSD, PCL/Coll as two - layered nanofibrous mat were designed with electrospinning. Bulge stem cells were isolated from rat vibrissa and cultured on two – layered nanofibrous mat with nanoparticles containing EGF and bFGF as growth factors. Nanoparticles containing EGF and bFGF were made with ionic gelation processes. EGF and bFGF release were analyzed with human EGF and bFGF Quntikine human ELIZA kit. Bulge stem cells were analyzed with Immunocytochemistry and flow cytometry. These cells were tracked with CM-Dill 7000C. Tracked cells were seeded on nanofibrous mat and grafted to rat skin. The healing process was evaluated with macroscopic observation on 7,14,21 and 28 days' post wounding. Hematoxylin - eosin and Trichromasons staining was done to

evaluate tissue remodeling and collagen synthesis. Real time PCR analysis performed to assess gene expression after 14 days of treatment.

Results: Results: This combination of nanofibrous mat with nanoparticles containing growth factors and rat hair bulge stem cells showed normal characteristics with desirable skin wound healing. Moreover, attachment and spreading of bulge stem cells on this nanofibrous composite was reported to be in an optimal condition. As well, in vivo evaluation demonstrated that full repaired skin had been observed on day 14 in the two-layered nanofibrous mat with bulge stem cells and nanoparticles containing growth factors group after being wounded.

Conclusion: Conclusion: The two-layered nanofibrous mat with bulge stem cells and nanoparticles containing growth factors could be considered as a suitable wound dressing of nanofibrous membranes in future in order to shorten healing time.

Keywords: Key words: hair follicle stem cells, nanofiber, wound healing, antibacterial agent.

Nanotechnology in cancer (Review)

Yegane Zahiri,[1,*] Roghayeh Gholizadeh Doran Mahalleh,[2]

1. Medical student, member of Young and Elite Researchers Club of Islamic Azad University, Zahedan, Iran
2. Department of laboratory sciences, Zahedan branch, Islamic Azad university, Zahedan, Iran

Introduction: Nanotechnology is the study of tools made by humans that have at least one range in the range of 1 to 1000 nanometers. To understand this scale, it should be noted that this range is equivalent to the size of a number of atoms and the size of intracellular structures. The problem of targeting a cancer drug, especially for a tumor, should be considered more and better in the future. Nanostructures can be filled with cancer drugs, and those that have targeting agents at their surface can be called nano-carriers. Nanocarriers have raised hopes for the proper and efficient delivery of tumor-specific drugs. The goal is the potential applications of nanotechnology in the field of cancer.

Methods: This review study relevant information from search databases Pub med ,Scopus ,Google Scholer & Magiran.Data analysis was performed qualitatively.

Results: Finally, nanotechnology will lead to the production of biomolecular sensors that are able to detect many biomarkers simultaneously and will be used to modify the process of diagnosis, prognosis, disease prognosis, and treatment. Two examples of special designs are nano-base and nano Both are coated with molecules attached to biomarkers. The nanoparticles are broken or tilted after binding to the biomarker. Using lasers, these failures are detected and tracked. The nanowires, after connection, undergo a change in their conductivity, and this change is electrically traceable. Both of these nanoparticles and nanowires change the method and speed of cancer detection.

Conclusion: Using nanotechnology, it may be possible to target specific drugs designed for a particular type of cancer, resulting in better treatment outcomes and fewer toxic side effects. This technology increases the ability to photography and identify biomarkers to improve the diagnosis. The use of biomolecular sensors can replace nanotechnology with a tissue resection method and eliminate the need for it.

Keywords: Nanotechnology, cancer, nanoparticles, nanowires and nanocarriers

Naringenin and Resveratrol Anti-tumor Impact on the Y79 Retinoblastoma by Affecting E/N-Cadherin and Galectin-3; Possible Synergistic Effect (Research Paper)

Seyyed Mojtaba Ghorani,[1,*]

1. Islamic Azad University, Tehran Medical Branch

Introduction: One of the detrimental features of retinoblastoma is highly invasiveness of this type of cancer; the ability to metastasize into distal organs even in the early stages. This phenomenon highlights the importance of experiments targeting this characteristic to diminish the disquieting outcomes. In this study our main aim was to assess the impact of naringenin and/or resveratrol (two main herbal extract with known anti-cancer properties) treatment on the important genes expression in the metastasis and cancer progression pathways in Y79 retinoblastoma cell line.

Methods: To attain the cytotoxicity dose of both reagents, MTT assay performed for 24 and 48 hours. The Y79 cells were then treated with lower dose compared with the IC50. To further investigate the synergistic effect of the compounds, concurrent treatment was also done. Finally the expression of E-cadherin, N-Cadherin, and Galectin-3 investigated in different samples by the aid of real-time PCR.

Results: According the MTT assay the 24 hours IC50 for resveratrol was about 100 µg/ml and 48 hours IC50 was about 50 µg/ml. Naringenin 48 hours IC50 calculated to be 100 µg/ml. Treatment of Y79 cells with naringenin, resveratrol, or the concurrent treatment down-regulated the N-Cadherin mRNA expression level. Treatment with resveratrol or the concurrent increased the expression level of the E-Cadherin and diminished Galectin-3 expression.

Conclusion: Resveratrol seems to be more toxic for Y79 cells compared with the naringenin. Two compounds didn't show significant synergistic effect. Both compounds exerts anti-metastatic effect on these cells by inducing N-Cadherin down-regulation. Resveratrol enhanced the expression of the E-Cadherin, along with the decreasing the Galectin-3 exerts even more anti-tumor activity, and can be proposed as a beneficial reagents in cancer immunotherapy.

Keywords: Retinoblastoma, Metastasis, E-Cadherin, N-Cadherin, Galectin-3

Neobaicalein, a flavonoid from the Scutellaria litwinowii Bornm. & Sint. ex Bornm exerts a apoptotic effect on human leukemic cell lines (Research Paper)

Elham Ramazani ,[1,*] Seyed Hadi Mousavi ,[2] Naser Vahdati-Mashhadian ,[3] Heydar Parsaee ,[4] Javad Asili ,[5] Seyed Ahmad Emami ,[6]

1. Medical Toxicology Research Centre, Mashhad University of Medical Sciences, Mashhad, Iran.
2. Medical Toxicology Research Centre, Mashhad University of Medical Sciences, Mashhad, Iran.
3. Medical Toxicology Research Centre, Mashhad University of Medical Sciences, Mashhad, Iran.
4. Department of Pharmacology and Pharmacological Research Centre of Medicinal Plants, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
5. Department of Pharmacognosy, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran.
6. Department of Pharmacognosy, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran.

Introduction: Neobaicalein is one of the rich flavonoid plants isolated from the roots of Scutellaria spp. In the present work, the cytotoxic activity and the related apoptosis mechanisms of neobaicalein from S. litwinowii Bornm. & Sint. ex Bornm on apoptosis-proficient HL-60 cells and apoptosis-resistant K562 cells was assessed and compared.

Methods: Cell viability, cell apoptosis, and caspase activity were measured using resazurin, propidium iodide (PI) staining and flow cytometry and synthetic pNA-conjugated substrates.

Results: Neobaicalein significantly reduced cell viability in a dose-dependent manner using the MTS assay. The IC50 values (μM) against HL-60 and K562 cells after 48 h treatment were 40.5 and 84.8 respectively. Also neobaicalein at 25, 50 and 100 μM for 48 h significantly increased the number of apoptotic cells in HL-60 and K562 cells. In addition, when K562 cells were exposed to neobaicalein for 48 h, the activity of caspases-3, -8 and -9 were elevated significantly ($P<0.05$).

Conclusion: It seems, neobaicalein might cause cytotoxicity and cell apoptosis through interaction with the different apoptosis-related proteins of apoptotic pathways in HL-60 and K562 cells. Thus, Neobaicalein may exert beneficial protective effect in slowing the progression of hematological

malignancies and warrants further investigation to find more therapeutic options.

Keywords: Neobaicalein, cell viability, apoptosis, caspase, Scutellaria litwinowii.

Neurologic complications as result of COVID-19 (Review)

Pedram Ghaderi,[1] Tannaz Haghgouie,[2,*]

1. University of Tabriz, Faculty of Veterinary Medicine, Department of Basic Sciences, Division of Pharmacology and Toxicology
2. University of Tabriz, Faculty of Veterinary Medicine, Department of Basic Sciences, Division of Pharmacology and Toxicology

Introduction: Since the emergence of severe acute respiratory syndrome coronavirus two (SARS-CoV-two) spread rapidly around the world. As respiratory complication is the primarily reported manifestation though rare, yet serious neurological complications are being frequently reported in the literature. selected coronavirus disease cases (COVID-nineteen) manifested neurologic complications. COVID-nineteen infection cause or even present with different neurological features including Encephalopathy, impaired consciousness, agitation, seizure, headache, anosmia, and neurodegenerative diseases. In this paper we provide a brief review of observed neurological manifestations associated with COVID-nineteen

Methods: We searched Pubmed , Google Scholar, ncbi using the keywords; “seizures”, SARS COV two’’, “COVID-nineteen” and "Encephalopathy". Search was limited to the English language manuscript only from twenty twenty to twenty twenty one. We identified two hundred twenty four research articles describing neurological complications in SARS-COV- two

Results: During the study period, 6147 people had confirmed COVID-19 in Fars province, Iran; 110 people died from the illness (case fatality rate 1.79%). During this time period, five people had seizures (seizure rate 0.08%). In four patients, seizure was one of the presenting manifestations, and in one person, it happened during the course of hospital admission. Two patients had status epilepticus. All patients experienced hypoxemia and four of them needed respirator. Two patients had related metabolic de-rangements and one had cerebrospinal fluid (CSF) lymphocytic pleocytosis. Brain imaging was abnormal in three patients. Four patients died. In a study conducted on 13 patients, Electroencephalography was obtained in eleven patients. Three patients had generalized slowing, and six patients showed focal areas of status epilepticus including the temporal lobe, frontotemporal regions and the centro-parietal regions Computed tomography (CT) head scan and magnetic resonance imaging (MRI) brain were obtained in all thirteen patients. One patient had MRI evidence of ventriculitis and encephalitis while one patient had MRI evidence of multiple, non-enhancing demyelinating lesions. In the remaining eleven patients, imaging studies showed no acute changes. Eight out of 13 patients underwent lumbar puncture. CSF COVID-PCR was reported positive in one patient though the

nasopharyngeal swab was reported negative. Six patients had negative CSF PCRs or were in institutions which could not test the CSF for COVID PCR. Three patients had elevated lymphocytes, one had elevated protein with otherwise normal CSF findings, and the 3 patients had no specific CSF findings. Lumbar puncture was not performed in 6 patients. There are several theorized pathways for SARS- COV-2 to enter the CNS. One of the chief targets of the SARS- COV-2 is the Angiotensin-converting-enzyme-2 (ACE-2) receptor cells. ACE-2 receptors are located on cells throughout the body, including the cardio-respiratory neurons of the brainstem, glial cells, basal ganglia, motor cortex, raphe, and endothelial cells of the brain. Once in the bloodstream, SARS-COV-2 can travel to infect the endothelial cells of the blood-brain barrier and then accumulate in the various ACE 2 heavy brain regions causing direct infection with neurological sequelae. A second route through which the SARS- COV-2 is theorized to enter the CNS is the olfactory nerve via the nasal cavity. It has been demonstrated that within seven days of infection, SARS-COV-2 can reach the CSF and brain through the olfactory nerve causing inflammation and demyelinating reactions with potential subsequent seizures. Removal of the olfactory bulb in mice has shown to restrict invasion of SARS-COV-2 into the CNS. Moreover, SARS-CoV-2 infection leads to a cerebral vascular injury that increases the risk of chronic brain damage, because of the collective damaging effect of multifocal cerebral or haemorrhage, endothelial and BBB dysfunction, and upregulation of pro-inflammatory cytokines within the brain In adults, post-viral anosmia is one of the major reasons for olfactory dysfunction in COVID-19, identified in up to 40% of infected patients. A study from Italy reports that around 33.9% of infected patients have either disturbance in taste or the olfactory system, whereas around 18.3% of infected patients experienced both disturbances. Anosmia was also reported as the first symptom in about 83% of infected patients.

Conclusion: The global problem of COVID-nineteen affected millions of human lives with a high infectivity rate. The major proportion of SARS-CoV-two infected patients showed more frequent respiratory disorders compared to neurological manifestations.Clinical, diagnostic, and epidemiological studies during acute and recovery phases are required for better diagnosis and management of the patients with COVID-nineteen

Keywords: COVID, Neurologic complications, Seizure, Encephalopathy

New insight for Uricase stabilization in the presence of taurine
(Research Paper)

Parisa Shahmoradipour,[1] Maryam Zaboli,[2] masoud torkzadeh_mahani,[3,*]

1. Department of Biotechnology, Institute of Science and High Technology and Environmental Sciences, Graduate University of Advanced Technology, Kerman, Iran
2. Department of chemistry, Faculty of science, University of Birjand, Birjand, Iran
3. Department of Biotechnology, Institute of Science and High Technology and Environmental Sciences, Graduate University of Advanced Technology, Kerman, Iran

Introduction: The enzyme urate oxidase (UOX) or uricase (EC 1.7.3.3) is an enzyme from the group of oxidoreductases that exists in a variety of organisms but does not exist in more advanced primates, including humans. This enzyme catalyses the oxidation of uric acid to 5-hydroxy isourate and hydrogen peroxide. Uricase can be used as a medicinal enzyme to reduce the level of uric acid in plasma. Despite of the high tendency of uricase to convert the substrate into a product, the low stability of this enzyme against heat has limited its usage. So far, many efforts have been made to improve the kinetic parameters and thermodynamic stability of the enzymes, such as enzyme point mutation, enzyme immobilization, and the use of additives. One of the most widely used additives to increase the stability of enzymes is the use of osmolytes. Taurine is one of the osmolytes that is used to stabilize the structure of proteins. Taurine is an organic acid with a molar mass of 125.14 g / mol found in natural food sources, biosynthesized in the body and also produced by chemical synthesis for commercial purposes. Taurine is derived from cysteine. In this study, UOX enzyme was recombinantly expressed and purified in a bacterial host and then the effect of taurine on the activity of UOX was investigated using the optimal response surface area (RSM) method.

Methods: Enzyme expression To express the recombinant UOX in E. coli cells of BL21 DE3 strain, the coding sequence of enzyme was subcloned in PET.28a vector and its expression was induced with IPTG (1 mM). After preparing the purified protein, the samples were loaded on 10% SDS-PAGE and the observation of a single band in the range of 35 kDa confirmed the expression of recombinant urate oxidase. The activity of urate oxidase enzyme can be measured according to the ability of the enzyme to break down uric acid and convert it to allantoin based on the reduction of uric acid absorption per minute at a wavelength of 293 nm. Response surface (RSM) method was used to achieve recommended optimal conditions including concentration of taurine, incubation time and temperature with taurine. RSM methodology The influence of the variables affecting the activity of the taurine-

treated UOX enzyme was investigated with a full fraction design. Four operating variables viz., incubation time, the taurine concentration and temperatures were examined. To optimize the three most significant factors, 18 full factorial central composite design (CCD) of RSM using Design-Expert software version 11 was employed.

Results: The quadratic equation was used to describe the response of the system (the activity of treated-UOX). The final model was shown in the following equation to predict the value of UOX activity: Activity= +1.49-0.0175 * A+0.1450 * B-0.1625 * C-0.1770 * AB=0.1295 * AC+0.1580 * BC+0.0683 * A2+0.0750 * B2-0.0087 * C2 where A, B, and C show incubation time, taurine concentration, and temperature, respectively. A positive sign was represented a synergistic effect, whereas the negative sign was indicated antagonistic effect on response. The optimum taurine concentration, temperature, and incubation time were found to be 450 mM, 28ºC, and 15 min, respectively, for achieving the maximum activity. All variables (taurine concentration, incubation time, and temperature) significantly affected the enzyme activity because significant changes in enzyme activity were observed for all combinations. The high F value, low P-value (< 0.0001), R2 and Adj-R2 = 1.00 and non-significant lack of fit show that the model was highly significant.

Conclusion: The value of adjusted R2 (1.0) shows that the total variations were explained with the obtained model. The non-significant lack of fit (<0.05) presented that the quadratic model was statistically significant for the response. The best conditions for UOX stabilization were achieved at 28ºC, 450 mM taurine concentration, and 15 min incubation time. The activity of UOX was obtained about 2.10 U/ml under the optimal conditions.

Keywords: uricase-taurine- stabilization

New perspective of deadly Scorpions venom (Review)

Narges Pashmforoosh,[1] Masoumeh Baradaran,[2,*]

1. Toxicology Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
2. Toxicology Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Introduction: Scorpions belong to an ancient group of the Arthropoda (1), the class Arachnida, which were reported from the collected fossil of the Silurian Period for the first time (2), and now around 2000 known species are included in this group (3). Scorpion stings after snake stings are causing human casualties from envenomation (4) and approximately, 2.3 billion people are at risk of scorpionism (1). Scorpions venom containing several peptides (5, 6) which are including, Neurotoxins, cytotoxins and antimicrobial peptides (5). These toxins target different ion channels, including sodium, potassium, chloride and calcium. Toxins extracted from the scorpion, on the other side, supply significant pharmacological tools for ion channels research and develop drug design (7) in different diseases including cardiac diseases (8), autoimmune diseases (9), and different types of cancers (10).

Methods: This review involves available literature about the significant number of scorpion venom toxins and peptides displaying properties that might be great candidates for drug development. Several databases, including PubMed, Web of Science, Science Direct, Springer Link, Wiley Online Library, and Google Scholar databases were searched to find, collect and classify all relevant data published from January 2000 to March 2020.

Results: Scorpion venom has proved a rich source of proteins and peptides, which are classified into different groups including; ion channels blockers, antimicrobial peptides, and cell proteins. These peptides are used for capturing prey and defence tools against predators. Besides, pharmacological properties of these peptides were confirmed, such as antimicrobial peptides, anti-cancers peptides, bradykinin potentiating-factors, autoimmune therapeutics, and analgesic effects in vitro and in vivo. Scorpions are found as a great and easy access origin of antimicrobial peptides. Scorpine (11), Stigmurin (12), Hp1090 (13), Smp76 (14), Vejovine (15), Meucin-49 (16) and some other antimicrobial peptides (AMP) are achieved from scorpions venom. Scorpion venom also could induce apoptosis, cytotoxicity, and effect on proliferation and immune system, thus it can be used in case of various cancers (17). ClTx (chlorotoxin) known as the first extracted chloride channel blocker (18, 19), and since its discovery, CTX has been linked to nanoparticles, radioisotopes and fluorescent molecules (20). Buthus martensi (BmK) venom (21), Bengalin (22), Margatoxin (MgTX) (23), BmK AGAP (24)

and many potent peptides might be used in cancer treatments. Nowadays, studies on the bradykinin potentiating-factors from scorpion venom were improved. The venom of Tityus serrulatus demonstrated the bradykinin potentiating factors (BPFs) and could influence on blood pressure through the inhibition of angiotensin converting enzyme activity and bradykinin receptor synthesis (25). Hypotensin (26), TsHpt-I (27), K12 (28), evidently are able to potentiate the bradykinin effect. In addition, OSK1 (29), Vm24 (9), ADWX-1 (30), HsTX1 (31) with properties of treatment of certain autoimmune diseases, and AngM1 (32), TsNTxP (33), Hetlaxin (34) via evidence of analgesic effects were reported from scorpions venom.

Conclusion: Venom glands of different species of scorpions are important sources of bioactive components that can be considered treasure. These vast resources are awaiting exploration. The importance of scorpion venom in producing and developing new drugs for the treatment of incurable diseases or for the production of drugs with greater therapeutic effect is undeniable. Although researchers have already discovered some of the vital potentials of scorpion venom, there is a lot of information in the scorpion venom that is waiting to be discovered. It is hoped that in the not-too-distant future, more useful drug discoveries will be presented to the world of science from this golden reservoir.

Keywords: Scorpion, pharmacological properties, neurotoxins, Antimicrobial peptides, ion channels.

Nickel nanoparticles: from toxicity to antibacterial activity (Review)

Yousef Alaee Mollabashi,[1,*] Peyman sefidi,[2] Elahe Khalili,[3]

1. Department of Biology, Tabriz Branch, Islamic Azad University, Tabriz, Iran
2. Department of Biology, Tabriz Branch, Islamic Azad University, Tabriz, Iran
3. Department of Biology, Ardanil Branch, Islamic Azad University, Ardabil, Iran

Introduction: Over time and through various studies around the world, nanotechnology has reached where we see it today. Nanoparticles are one of the most valuable products in the development of nanotechnology. Nanoparticles of silver, gold, zinc, manganese, nickel, etc. are among the nanoparticles that have been produced and studied so far. The typical size of these particles is between 1 nanometer to 100 nanometers, but in some studies, this size is more than 100 nanometers. By reducing the particles size from micrometres to nanometers, extensive and important changes in the physical and chemical properties of the particles occur. One of the most important of these changes is the size of the surface to the volume. Due to their small size, nanoparticles can penetrate tissues, cells, biological structures, etc. in the human body, animals, pathogens, etc. and be effective. For many years, for various reasons, such as small size, nanoparticles charge, etc., concerns have been raised about the toxicity and dangerousness of such particles, which should be subjected to strict considerations and controls for use in clinical cases related to humans. However, regarding the antimicrobial properties of nanoparticles, various studies have been performed on particles such as silver, copper, zinc, iron, etc., and it has been proven that due to the effect on the cell wall and cell membrane of pathogens, the effect on the respiratory chain, induced planned death, and so on. Nickel in the periodic table of elements is a hard metal with a white-silver colour. Nickel nanoparticles are also black and spherical, which has been effective against various bacteria. However, in addition to this antibacterial property, these nanoparticles have toxic properties and side effects such as induction of oxidative stress, production of free radicals, etc. In this study, our aim is to provide an overview of the antibacterial and toxic properties of nickel nanoparticles.

Methods: Using keywords related to the purpose of this study, such as nickel nanoparticles and antibacterial activity of nickel nanoparticles and etc, we applied to find the desired references without applying a specific time interval.

Results: Endocytosis (active) and diffusion (passive) methods are used to adsorb nanoparticles into cells. According to the NTP and the IARC in previous years, nickel is carcinogenic element and is in the number one group. In one study, researchers suggested that one of the reasons for the

decrease in catalase activity was the accumulation of free radicals and so on. On the other hand, nickel nanoparticles in high and low doses cause fluctuations in the concentration of catalase in the liver, which may be due to tissue damage caused by nanoparticles. In another study, the introduction of nickel nanoparticles into the body of the study model increased the levels of ROS and MDA. Various studies can be mentioned on the antimicrobial properties of nickel nanoparticles. The results of a study showed that the concentration and duration of contact of nickel nanoparticles with the pathogen are effective on its antibacterial properties. In another study, nickel nanoparticles were used on the biofilm of mupirocin-resistant Staphylococcus aureus and were able to kill it.

Conclusion: Further studies on the antimicrobial properties and negative effects of these nanoparticles can lead to more and better improvements.

Keywords: Nickel nanoparticles, Toxicity, Antibacterial

Niosomes: Promising nanocarriers as co-delivery systems for cancer therapy (Review)

Navid Mousazadeh,[1] Negin Mousazadeh,[2] Hamid Rashidzadeh,[3,*]

1. Department of Medical Biotechnology, School of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran
2. Department of Nursing, School of Nursing and Midwifery, Ardabil University of Medical Sciences, Ardabil, Iran
3. Cancer Gene Therapy Research Center, Zanjan University of Medical Sciences, Zanjan, Iran

Introduction: Over the last decade, development of nanomaterials for a variety of biomedical applications, especially for the diagnosis and treatment of diseases have received great attention (1). Biocompatibility, non-toxicity, high drug loading capacity, controlled release of cargo are accounted for the characteristics of an ideal drug carrier for smart drug delivery systems (2). In the context of drug nanovehicles for cancer therapy, various types of nanosystems such as nanogels, cubosomes dendrimers, carbon nanotube, liposomes nanospheres, nanocapsules, and niosomes have been developed so far (3). Among these carriers, niosomes regards as a propitious drug vehicle and could be fabricated by self-association of nonionic surfactants and cholesterol in an aqueous phase. Interestingly, it possess great stability, biosafety, long shelf-life and biocompatibility as its structures and components are similar to cell bilayer. Besides these they are nonimmunogenic, biodegradable and could deliver its cargo into the intended site of action in a controlled and/or sustained manner (4, 5). Niosomes owing to its unique structure could encapsulate both hydrophilic and lipophilic drugs as new classes of effective drug delivery systems.Cancer as group of disease is still one of the leading causes of death worldwide, leading to a steady increase in the economic and financial burden on healthcare and treatment (6). According to the global cancer statistics, in 2020, aproximately 19.3 million new cases of cancer along with 10 million deaths occurred (7). The current and common method of cancer treatment is chemotherapy. Therapeutic effect of many anticancer drugs due to their weak penetration into tumor tissue and severe side effects are highly limited. Various attempts have been made to overcome these shortcomings, such as implementation of niosomes as a unique drug delivery system (4). The aim of the current work is to review the most recent advances and applications of niosomes in the treatment of cancer with particular emphasis on recent studies in co-delivery of drugs for cancer therapy.

Methods: In this review article the key words of niosomes and combination therapy, cancer were searched in various databases such as Google scholar and some exciting novel articles were selected.

Results: It was found that niosomes are promising nanocarriers in multi-drug delivery applications. Akbarzadeh and colleagues developed a folic acid-functionalized niosome containing curcumin (CUR) and letrozole as a potential drug nanovehicles for the treatment of breast cancer cells. The in vitro cell viability assay revealed that the fabricated nanovehicles exhibited great biocompatibility with HEK-293 normal cells, whereas, displaced significant cytotoxicity activity toward MDA-MB-231and MCF-7 cell lines due to the modification of niosomal formulation with targeting agent of folic acid (8). In another research Abtahi et al. fabricated niosomal formularion containing microRNA-34a (miR-34a) and CUR for effective cancer therapy. The results showed that fabricated niosamal formulation (NCur-miR) represented superior anticancer potential and cellular uptake in cancer cells and suppressed tumor growth compared to other groups (9). Additionally, Maniam et al. showed that co-encapsulation of tocotrienols and gemcitabine in the niosomal formulation exhibited remarkable cytotoxicity activity on cell pancreatic cancer (10). Rathee and colleagues revealed that co-delivery of TLR7 agonist with IDO-inhibitor by nisomal formulation could be further investigated in cancer vaccine as well (11). Additionally, Ghaffari and colleagues developed cationic niosomes decorated with PEG moieties for co-delivery of miRNAs. In this regard both niosomes containing miR-16–1 and miR-15a was prepared and its potential efficacy in prostate cancer cells were evaluated. The results indicated that the niosomal formulation containing both miRNAs could effectively downregulate the Bcl-2 gene, induce more apoptosis and resulted in favorable outcomes in treatment of prostate cancer (12).

Conclusion: Niosomes as new classes of drug vehicles offer several advantages compared with other nanomaterial-based drug carrier in design of smart and effective drug delivery vehicles. As they could potentially deliver either hydrophilic and lipophilic drugs or both of them in which could be harnessed in combination therapy and co-delivery of chemotherapeutics. Several studies proved that niosomes as very promising tools can be utilized for combination therapy in combating cancer.

Keywords: niosomes, combination therapy, co-delivery, nanocarrier, cancer therapy

Novel nano delivery for CRISPR/Cas system delivery instead of traditional methods (Review)

Helia Ramezani ,[1,*] Hanieh Ataollahi,[2]

1. Faculty of Biological Science, Department of Biotechnology, Islamic Azad University Tehran North Branch, Tehran, Iran.
2. Faculty of Biological Science, Department of Biotechnology, Islamic Azad University, North Tehran Branch, Tehran, Iran.

Introduction: Introduction: In recent years, clustered regularly interspaced short palindromic repeat (CRISPR) /CRISPR-associated (Cas) genome editing systems have become one of the most powerful platforms for basic biomedical research and therapeutic applications. CRISPR/Cas systems are adaptable immune mechanisms of many bacteria and archaea to protect themselves from invading nucleic acids. Since its first application in mammalian cells in 2013, the CRISPR / Cas system, based on RNA guided nucleases, has revolutionized the way genome editing is done. In previous decades, the generation of disease models was an extremely slow and expensive process, requiring complex manipulation of embryonic stem cells, as well as endless reproduction of mice to achieve the desired phenotype and genotype. However, following the emergence of the CRISPR / Cas9 system, new disease models have been developed with unprecedented speed and precision due to the simplicity and flexibility of these systems. Despite the aforementioned merits, efficient delivery may likely become the main hurdle in the eventual application and clinical translation of the CRISPR/Cas9 system. Currently, the strategies of CRISPR/Cas9 delivery are mainly based on physical approaches (electroporation, microinjection, hydrodynamic injection, etc.) and viral vectors (lentivirus, adenovirus (Ad), adeno-associated virus (AAV), etc.). have achieved successful therapeutic efficacy via precise modification of the genome and exceeded previous genome engineering methods owing to its versatility and simplicity. Rapid expansion in biomedical research has benefited from this newly emerged technique, such as genetic diseases treatment, cancer characterization, and plant improvement. However, the key challenge is the efficient delivery of CRISPR components in vivo and nanotechnology plays an indispensable role in nonviral gene delivery. Polymer polyethylenimine (PEI), a golden standard for gene delivery, was utilized to deliver large-sized plasmids with relatively high efficiency both in vitro and in vivo compared to virus carriers. Moreover, polymer polyethyleneimine-(PC)-cyclodextrin was synthesized to deliver CRISPR/Cas9 plasmid with much lower cytotoxicity compared to PEI 25K.

Methods: Method: This study is a review study that conducted in 2021. The data of this study using the keywords “CRISPER/Cas”; “Drug delivery system and CRISPER” at “ScienceDirect”; “PubMed”; “Springer” databases were

collected and were analyzed. Articles were opted and were utilized based on their relevance owing to title and abstract.

Results: Result: Based on several new methods of CRISPR/Cas system delivery mentioned in the new research, instead of using common delivery systems, they are more operational. These nano-drug delivery systems include different types of polymer nanoparticles, liposomes, gold nanoparticles, conjugated cell-penetrating peptide (CPP) modified nanoparticles, and cell membrane-derived nanoparticles. In addition, it has recently been reported that a new CRISPR/Cas12b system has been developed that can significantly reduce the off-target effects of human genome editing. In addition, Cas9/sgRNA RNP is considered more advantageous because it has higher safety and fewer off-targets compared to the other two delivery methods (CRISPR/Cas9 plasmid or Cas9 mRNA/sgRNA hybrid). Controlling the activity of Cas9 ribonucleoprotein within a specific time window can effectively prevent Cas9 from being overactive, thereby reducing side effects and improving safety.

Conclusion: Conclusion: In the future, using new drug delivery systems rather than CRISPR/Cas9 delivery strategies that are mostly dependent on physical approaches will have a privileged role in clinical trhapetics. Furthermore, because of its versatility and simplicity, the genome-editing tool, clustered regularly interspaced short palindromic repeats (CRISPR)/Cas9 system, could achieve successful therapeutic efficacy through precise genome modification and outperformed previous genome engineering methods.

Keywords: Keywords: CRISPER/Cas9, Nano drug delivery, Genome editing

Novel NLR, PLR and HPR biomarkers for Diagnoses of Acute lymphoblastic leukemia (Research Paper)

Mohammad Reza Javan,[1,*] bahar moghimian,[2] Seyyede Fatemeh Shams,[3] Mehrnaz Abdolalian,[4]

1. Blood Transfusion Research Center, High Institute for Research and Education in transfusion Medicine, Tehran, Iran.
2. Thalassemia & Hemoglobinopathy Research Center, Health Research Institute, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
3. Blood Transfusion Research Center, High Institute for Research and Education in transfusion Medicine, Tehran, Iran.
4. Blood Transfusion Research Center, High Institute for Research and Education in transfusion Medicine, Tehran, Iran.

Introduction: Acute lymphoblastic leukemia (ALL) can affect both B and T cell lines at any stage of hematopoiesis. It is the most common leukemia in children and the second most common cancer in childhood. Genetic mutations in ALL cause uncontrolled cell proliferation and prevent normal cell differentiation, which can lead to death if left untreated. Therefore, timely diagnosis and treatment is very important. Complete blood count (CBC) can be a simple but valuable initial test to diagnose ALL.

Methods: In this study, 54 ALL patients (Mean ages: 5.29) and 29 healthy controls (Mean ages: 5.53) were evaluated and compared in terms of hematological parameters including Platelet to lymphocyte ratio (PLR), neutrophil to lymphocyte ratio (NLR) and hemoglobin to platelet ratio (HPR). Cytogenetics and immunophenotyping were analyzed between two groups.

Results: In the analysis of hematological factors between the case and control groups, all indices except Lymphocytes showed a statistically significant relationship (P-Value<0.05). In the analysis of hematological factors between the B-ALL and T-ALL groups, only WBC and ESR showed a statistically significant relationship (P-Value<0.05). The ROC curve was generated to select the appropriate cutoff values for NLR, PLR and HPR based on analysis. NLR and PLR has a cut off value 0.50 and 62.24 respectively and can be a good biomarker for distinguishing ALL from normal people. HPR value was significant between case and control groups, but it was not a suitable biomarker for distinguishing patients from the control group based on ROC analysis.

Conclusion: CBC is a simple and valuable test for early detection of ALL, and the new PLR and NLR markers are good hematologic markers for ALL diagnosis.

Keywords: Acute lymphoblastic leukemia, Platelet to lymphocyte ratio, Neutrophil to lymphocyte, CBC

OCT4B1 up-regulation in BM-MSCs and HSFPI3 after Nanocurcumin Treatment (Research Paper)

Zahra Abbasy,[1,*]

1. Faculty of Medicine, Kashan University of Medical Sciences, Kashan, Iran

Introduction: The tumor recurrence is a big dilemma which may be neglected especially in vitro experimental designs. The crucial and vital player in this phenomenon is the tumor initiating cells (TICs). OCT4 is widely appreciated non-cell surface for TICs, dedicates detrimental properties to these cells including self-renewal, epithelial mesenchymal capacity, and drug resistance. OCT4 and its partners Sox2 and Nanog are up-regulated in stem cells; on the other hand normal stem cells are more resistant to various herbal remedies like curcumin. Based on these facts our main aim in this study was to investigate the alteration of the mentioned genes expression after curcumin treatment in human bone marrow mesenchymal stem cells (hBM-MSCs) and non-tumor fibroblast cells (HSFPI3).

Methods: MTT assay was performed to calculate the effective concentration of curcumin. To confirm the apoptosis induction in these cells after treatment with curcumin, Annexin V-PI was applied. To assess the expression level of OCT4 and Nanog, real-time PCR performed to quantify the alteration of the mRNA expression of the mentioned genes after treatment in hBM-MSCs and HSFPI3.

Results: Curcumin could not induce significant apoptosis in hBM-MSCs and HSFPI3 even after 24 and 36 hours treatment in a toxic concentration for cancerous cells. After 36 hours treatment with DNC, the mRNA expression level of Oct4-B1 in both cells enhanced significantly compared with the untreated samples. In HSFPI3 cells Nanog mRNA expression level increased either after this treatment.

Conclusion: non-tumor cells are more resistant to the curcumin treatment compared with the cancerous cells. This is at least partially due to the different expression pattern results in these cells post treatment with this reagent. Pluripotent markers including Oct4-B1 and Nanog are proposed to play important role in this non-tumor cells curcumin resistance.

Keywords: cancer stem cells, pluripotent markers, cancer cells, non-tumor cells, Nanog

Oligonucleotide-based drug delivery: challenges and opportunities (Review)

parastookazempour,[1,*] Nazanin Jabellat,[2] Anahita Ataie,[3] Razieh Moazeni,[4] Seyyed Ebrahim Moosavifard,[5]

1. Student Research Committee, Jahrom University of Medical Sciences, Jahrom, Iran
2. Student Research Committee, Jahrom University of Medical Sciences, Jahrom, Iran
3. Student Research Committee, Jahrom University of Medical Sciences, Jahrom, Iran
4. Student Research Committee, Jahrom University of Medical Sciences, Jahrom, Iran
5. Student Research Committee, Jahrom University of Medical Sciences, Jahrom, Iran

Introduction: The majority of human sicknesses are inspired through genetic factors. Therefore, one healing avenue, gene therapy, substitutes the disease-related gene with the 'healthy' model of the gene or gene products. The first authorised human gene therapy treatment was approved in 1990. Oligonucleotides are nucleic acid polymers with the capacity to deal with or control a huge variety of diseases. Although most oligonucleotide therapies have focused on gene silencing, other strategies are being pursued, including splice modulation and gene activation. As of January 2020, ten oligonucleotide pills have obtained regulatory approval from the FDA. These molecules have potential therapeutic uses in a variety of indications, with several oligonucleotide drugs recently approved. However, despite recent technological advances, obtaining efficient oligonucleotide delivery, particularly into extrahepatic tissues, remains a significant translation limitation. This Review will offer an outline of oligonucleotide-primarily based totally drug systems.

Methods: A systematic search was conducted to identify studies published in multiple databases (Science Direct, Pubmed and google Scholar) by 2021, and recently published abstracts were also reviewed using the keywords oligonucleotides, oral drug, and drug delivery.

Results: Oligonucleotides are used to modulate gene expression via RNAi, splice modulation, RNase H-mediated degradation of cleavage targets, inhibition of non-coding RNA and gene activation methods. They also have been used for the past two decades in the PCR primers (polymerase chain reaction), RNA, siRNA and antisense studies, molecular diagnostics, gene therapy, microarrays, hybridization fluorescence in situ (FISH) and fluorescence resonance energy transfer. There are wide techniques for

oligonucleotide delivery. One is to include the oligonucleotide into a few shape of nanocarrier that then determines the tissue distribution and mobile interactions of the oligonucleotide. The different is to chemically adjust the oligonucleotide itself, maximum usually with a concentrated on ligand, whilst retaining the molecular nature of the conjugate.

Conclusion: proteins, lipids, and lipoproteins that were used as drugs and excipients. At the start of this studies area drug loading, enzymatic safety and cell uptake had been key troubles accompanied through extra complicated programs along with pulmonary drug transport or immune-modulation and vaccination. Summarizing the current knowledge in the field of protamine oligonucleotide nanoparticles, this drug delivery system provides significant flexibility in formulation and application

Keywords: Drug delivery- oligonucleotid -genetic

Optimizing lentivirus production for CAR T cells development (Research Paper)

Zahra Sharifzadeh,[1,*] Shafieeh Mansoori,[2] Soheila Ajdari,[3] Mohammadali Shokrgozar,[4] Shahriyar Abdoli,[5] Mohsen Basiri,[6]

1. Immunology Department, Pasteur Institute of Iran, Tehran, Iran
2. Immunology Department, Pasteur Institute of Iran, Tehran, Iran
3. Immunology Department, Pasteur Institute of Iran, Tehran, Iran
4. National Cell Bank of Iran, Pasteur Institute of Iran, Tehran, Iran
5. School of Advanced Medical Technologies, Golestan University of Medical Sciences, Gorgan, Iran
6. Department of Stem Cells and Developmental Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran

Introduction: Immunotherapy with chimeric antigen receptor T (CAR T) cells is one of the most successful approaches of cancer therapy. Recently, five CAR T cell drugs are approved for relapsed or refractory hematological malignancy and multiple myeloma treatment. To produce CAR T cells, T lymphocytes are genetically modified ex vivo to express a CAR receptor, conferring them the ability to identify and destroy cancerous cells. Although there are some techniqies for gene engineering of T cells, viral vectors are the most efficient one. All marketed CAR T cell therapies rely on viral vectors (lenti or retro virus) to transduce the therapeutic chimeric antigen receptor (CAR) into T lymphocytes. However, high titer virus production for transduction to Jurkat or primary T cells is a challenge. To achieve this goal Primarily, transfection rate must be high. In addition, gene editing with viral vectors is more expensive than the other methods because it requires a large amount of an efficient transfection reagent which typically are expensive. Therefore, the choice of the desired transfection reagent and optimizing transfection parameters can tackle the challenges. Here, we have used polyethylenimine (PEI) 25000 as a cheap transfection reagent and considered some parameters such as pre-coating plate, DNA: PEI ration, and DNA/PEI complex volume for optimization. A TGFb CAR T cell, which was already developed in our lab, used for the experiments.

Methods: The TGFb CAR contains a C-myc tag in the outer part of the CAR, which is used to assess the surface expression of the TGFb CAR, and a mcherry marker on the cytosolic part. The TGFb CAR was replaced at GFP site of the pLOX plasmid. pLOX is a viral vector plasmid containing GFP marker that was used as a control. The second generation viral vector including the TGFb CAR/or pLOX, as a transfer vector, pSPAX2 and pMD2G plasmids were used for virus production. The total DNA of 4.5 µg was considered as a constant parameter. The used PEI reagent volumes were 4.5

µl and 9 µl, and DNA/PEI complex volume was set on 100 µl and 200 µl. To pre-coating, the 6-well plates were coated with FBS 10% one day before transfection. On the transfection day, 1.2X106 LentiX 293T cells counted and co-transfected with all three plasmids according to the designed test. 48 h after, CAR expression were assessed using fluorescent microscope and flowcytometery. The virus titration was determined using the control cell and the following formula:

Results: Hek293T cells were co-transfected with viral plasmids and PEI 25000 according to the corresponding test set. No significant toxicity was observed when PEI 25000 with 1:1 and 1:2 DNA:PEI ratio was used. TGFb CAR was successfully expressed in Hek293 T cells well after transduction. The best transfection rate for pLOX and TGFb CAR were included 1 DNA: 2 Reagent ratio, with the pre-coating plate, and 200 µl DNA/PEI complex. These conditions exhibited high titer virus production compared to other ones as well.

Conclusion: In this study, the optimized conditions were determined for co-transfection of TGFb CAR using PEI 25000 reagent to reach high titer virus production and reduce the costs of CAR T cells development using viral-based gene editing systems. Several transfection reagents such as Lipofectamin, Screenfect A and Turbofect have been used that have shown high transfection efficiency and less toxicity. However, these reagents were expensive and it is a limiting factor for gene delivery via viral vectors. PEI25000 can be recruited as a cheap reagent with no toxicity under the optimized conditions.

Keywords: Lentiviral Transduction, Optimization, PEI, Chimeric Antigen Receptor

Optimizing photodynamic therapy by aluminum phthalocyanine chloride-nanoemulsions against breast cancer (Research Paper)

ZAHRA JALALI ADERGANI,[1,*]

1. 1- Department of Biochemistry, Falavarjan Branch, Islamic Azad University, Isfahan, Iran 2- Department of Biology, Falavarjan Branch, Islamic Azad University, Isfahan, Iran

Introduction: Introduction: Cancer is one of the serious burdens worldwide that wide-ranging efforts are being made to combat it. Among different types of cancer, breast cancer is one of the most common cancers in women. However, conventional treatments have not been very amenable to this problem. Photodynamic therapy (PDT) is considered as a new non-invasive method that causes minimal damage to the non-tumor tissue surrounding the lesion. This method requires three components of light, photosensitizer (PS), and oxygen. Absorption of photons by PS lead to excitation of the molecule, producing reactive oxygen species (ROS) and free radicals, which can damage the cellular organelles and cause cell death. In this study, the photodynamic therapy conditions using a nanoemulsion system containing aluminum phthalocyanine chloride (NE/AlClPc) were optimized against breast cancer in vitro. Then, anticancer activity of the system in the optimized conditions was evaluated against normal cells.

Methods: Methodology: Different parameters of photodynamic therapy conditions, i.e. dark incubation times (2, 4, 10, and 24 hr), PS concentration (10, 20, 50, and 90 µg/ml), and laser dose (1.25, 2.5, 5, and 20 J/cm2) were evaluated on breast cancer cell line of MCF-7, using one-factor-at-a-time (OFAT) experiments. The optimization was carried out in three steps. In the first step, effect of different incubation time was studied, while the drug and laser dose were kept constant in 50 µg/ml and 2.5 J/cm2, respectively. In the second step, the PS concentration was optimized, while incubation time and laser dose were hold constant in the optimized incubation time resulted from the first step and 2.5 J/cm2, respectively. In the third step, in the optimized conditions obtained from previous steps, the different laser dose was studied on reduction of viability percentage of the cancer cells. Finally, the viability of the normal cells was evaluated in the optimized conditions.

Results: Results: The results showed that the optimized conditions of dark incubation time, PS concentration, and laser dose were 4 h, 50 µg/mL, and 2.5 J/cm2, respectively. Under these conditions, the viability percentage of cancerous cells in the presence of laser and dark conditions were 41.8% and 76.8%, respectively. The effect of PS in the presence of laser in reduction of the cancerous cells viability percentage was significant ($p < 0.05$). In addition, the normal cells under the optimized conditions in the presence of laser

showed 67.6% of viability, which is significantly ($p < 0.05$) higher than the cancerous cells in the same conditions.

Conclusion: Conclusion: According to the results, the optimized conditions were effective in reduction of viability of the cancerous cells, while were not toxic for the normal cells. The current results were also showed that the NE/AlClPc used in PDT had significant effects on the cell death of the cancer cells.

Keywords: Photodynamic therapy, Breast cancer, Optimization, aluminum phthalocyanine chloride, Nanoemulsions

Optimizing photodynamic therapy using nanoemulsion systems containing aluminum phthalocyanine chloride against melanoma skin cancer (Research Paper)

Malahat Rezaee,[1,*] Mina Bakhtiary,[2] Ramesh Monajemi,[3]

1. Department of Biochemistry, Falavarjan Branch, Islamic Azad University, Isfahan, Iran
2. Department of Biochemistry, Falavarjan Branch, Islamic Azad University, Isfahan, Iran
3. Department of Biology, Falavarjan Branch, Islamic Azad University, Isfahan, Iran

Introduction: In recent days, skin cancer is seen as one of the most hazardous form of the cancers found in humans. Skin cancer is found in various types such as melanoma, basal and squamous cell carcinoma among which melanoma is the most unpredictable. However, conventional treatments have not been very successful to this problem. Photodynamic therapy (PDT) is a minimally aggressive therapeutic modality approved for clinical treatment of several types of cancer and non-oncological disorders. PDT employs a photosensitizer (PS) and visible light in the presence of oxygen, leading to production of cytotoxic reactive oxygen species, which can damage the cellular organelles and cause cell death. In this study, the photodynamic therapy conditions using a nanoemulsion system containing aluminum phthalocyanine chloride (NE/AlClPc) were optimized against melanoma skin cancer in vitro. Then, anticancer activity of the system in the optimized conditions was evaluated against normal cells.

Methods: Different parameters of photodynamic therapy conditions, i.e. dark incubation times (2, 4, 10, and 24 hr), PS concentration (10, 20, 50, and 90 µg/ml), and laser dose (1.25, 2.5, 5, and 20 J/cm2) were evaluated on mouse melanoma cancer cell line of B16-F0, using one-factor-at-a-time (OFAT) experiments. The optimization was carried out in three steps. In the first step, effect of different incubation time was studied, while the drug and laser dose were kept constant in 50 µg/ml and 2.5 J/cm2, respectively. In the second step, the PS concentration was optimized, while incubation time and laser dose were hold constant in the optimized incubation time resulted from the first step and 2.5 J/cm2, respectively. In the third step, in the optimized conditions obtained from previous steps, the different laser dose was studied on reduction of viability percentage of the cancer cells. Finally, the viability of the normal cells was evaluated in the optimized conditions.

Results: The results showed that the optimized conditions of dark incubation time, PS concentration, and laser dose were 4 h, 50 µg/mL, and 2.5 J/cm2, respectively. Under these conditions, the viability percentage of melanoma

cells in the presence of laser and dark conditions were 34.22% and 73.71%, respectively. The effect of PS in the presence of laser in reduction of the cancerous cells viability percentage was significant ($p < 0.05$). In addition, the normal cells under the optimized conditions in the presence of laser showed 71.71% of viability, which is significantly ($p < 0.05$) higher than the cancerous cells in the same conditions.

Conclusion: The results showed that the optimized conditions were effective in reduction of viability of the melanoma skin cancer cells, while were not toxic for the normal cells. The current results were also depicted that the NE/AlClPc used in PDT had significant effects on the cell death of the melanoma skin cancer cells.

Keywords: Photodynamic therapy, Melanoma, Optimization, Aluminum phthalocyanine chloride, Nanoemulsions

Oral Manifestations of Vitamin Deficiency (Review)

Shirin Saravani,[1,*] Hamideh Kadeh,[2]

1. Oral & Dental Disease Research Center, Department of Oral & Maxillofacial Pathology, Zahedan University of Medical Science, Zahedan, Iran
2. Oral & Dental Disease Research Center, Department of Oral & Maxillofacial Pathology, Zahedan University of Medical Science, Zahedan, Iran

Introduction: The oral cavity is a unique anatomical environment that can show the early signs of eating disorders or other systemic diseases. Vitamins and minerals are needed for rapid and proper cellular turnover of the oral mucosa. B complex vitamins (2,3,5,6,7,9,12) and vitamins A, C, D, E have an important relationship with oral health. Vitamin A deficiency leads to angular cheilitis and atrophy and dryness of the oral mucosa. Vitamin B deficiency is associated with glossitis, stomatitis, and oral ulcers such as burning erythematous macules. Vitamin C deficiency leads to refractory gingivitis. Deficiency of vitamins A and C together causes generalized gingival swelling, spontaneous bleeding, ulcerations, loosing teeth, increased severity of periodontal infections, and bone loss. Vitamin D deficiency is associated with bone hypomineralization and an increased risk of jaw fractures. It also increases the prevalence of periodontal disease (gingivitis and periodontitis) and increases the risk of infection, malignancy and autoimmune disease. Adequate vitamin D can delay the formation of dental caries by delaying its onset and progression. The most common oral manifestation of vitamin K deficiency is gingival bleeding. In this study, we try to review the research done on oral manifestations due to vitamin deficiency.

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Keywords: Malnutrition, Vitamins, Mouth, Oral pathology

Overview on Cancer stem cells؛Pi3K/ERK signaling, MEK/ERK signaling. (Review)

mobina movahed,[1] ali malekpour,[2] danyal farajnia rick,[3,*] zhila shokrian,[4]

1.
2.
3. Secretary of Sarab University Laboratory Science Association
4.

Introduction: Cascal stem cells (CSCs) are subcutaneous of cells in the tumors that have the characteristics of self-renewable stem cells, differentiation and the ability to decrease parent tumor during the host transplantation. Stem cells (CSCs), or tumor initiator cells, are involved in the onset, progression, and spread of cancer to organs.CSCS has also reported over the years the styles of tumors including leukemia, thoracic, bacterial brain and lung, resulting in preserved stem cell characteristics and their role in treatment. AML was one of the earliest diseases in which the population of depleted stem cells was abolished into stem cells (LSCs), which eventually led to the population of stem cells from bone cancer, which led to a very large population.CSCs have been identified in human cancers through various biomarkers. CSCs can be isolated by combining specific biomarkers that are mostly located at the cell surface. The primary isolation techniques are fluorescence-activated cell sorting (FACS) and magnetic cell sorting (MACS). CSCs were first identified in leukemia and then isolated in the 1990s through spurface expression of CD34 + and CD38.CSCs can produce tumors through self-development and differentiation of multiple cell subspecies. The phenotype (leukemic stem cell) of LSCs has been described as CD34 + / CD38- and can be derived from distinct hematopoietic stem cells and distinct hematopoietic progenitor cells. CD133 is the most common CSC surface marker in various cancers, and specific antibodies / immunotoxins against CD133 have been successfully developed to selectively eradicate them. CD133 expression is detected in 22 of 82 cell types from 44 normal human tissues. PODXL-1 (Podocalixin-like protein) is rarely expressed in normal tissue cells, but is strongly expressed at the level of undifferentiated hESCs. PODXL-1 is also expressed in hematopoietic progenitor cells and leukemia. CD49f (integrin alpha 6) is strongly expressed in hESCs and is significantly reduced by embryonic body formation. Studies show that CD26 is a CSC marker for leukemic stem cells and colorectal CSCs All pathways respond to extracellular and intracellular signals to control survival, proliferation, motility, and metabolism, and are activated .The PI3K-Akt-mTOR pathway has been extensively studied in normal and malignant cells. The PI3K / PTEN / Akt / mTOR pathway plays an important role in predisposing to leukemia. Overactive PI3K-Akt pathway is involved with progression in most tumor types.The PI3K-Akt pathway is one of the most important pathways involved

in survival and proliferation.The involvement of the PI3K-Akt pathway in cancer development and progression has been extensively studied and Akt1 has been identified as a carcinogen.The drug target of the PI3K-Akt-mTOR pathway with specific inhibitors suppresses the growth of leukemic cells.The Ras-Raf-MEK-ERK pathway strongly interacts with the PI3K-Akt-mTOR messaging pathway, showing each other's positive and negative tuning, and together regulating several central cell functions. Ras-Raf-MEK componentsThe -ERK path also shows the positive adjustment of the PI3K-Akt-mTOR path.

Methods: Based on the study of authoritative articles and books as well as search for words such as;csc markers, separation methods, csc-related signaling pathways from scientific sites such as PubMed, Google Scholar, NCBI We used publications published from 2015 to 2021.

Results: With further studies, we finally came to this conclusion. Stem cells (CSCs) or tumor-initiating cells (TICs) are responsible for the onset, progression, and spread of cancer to distant organs.CD133 is the most common CSC surface marker in various cancers, and specific antibodies / immunotoxins against CD133 have been successfully developed to selectively eradicate them.Overactive PI3K-Akt pathway is involved with progression in most tumor types.The Ras-Raf-MEK-ERK pathway strongly interacts with the PI3K-Akt-mTOR messaging pathway Path convergence on substrates.

Conclusion: In this study, we examined the cancer stem cells of CSCs, their diagnostic markers from natural stem cells as well as their isolation methods, and the impact of the PI3K / ERK and MEK / ERK signaling pathways. We discussed the development or inhibition of CSCs activation.And we see that the marker CD133 is one of the most common markers for CSCs. And further activation of the pi3k / erk pathway is involved in the transformation of normal stem cells into CSC cancer cells.

Keywords: Cscs, CSC detection markers, CSC separation methods, Pi3K/ERK signaling, MEK/ERK signaling

Overview on the SMAD/non-SMAD of TGF-b signaling pathway: cancer and mutation (Review)

zhila shokrian,[1] mobina movahed,[2] ali malekpour,[3] danyal farajnia rick,[4,*]

1.
2.
3.
4. Secretary of Sarab University Laboratory Science Association

Introduction: Compared to other growth factors, cell type, and environment, almost all TGF-b family proteins promote cell growth and proliferation. Beta growth factor (TGF-b) is a multifunctional polypeptide and its roles include controlling a significant number of cellular mechanisms and biological metabolisms. For an overview of the signaling pathway, TGF-b molecules bind to membrane receptors that have Ser / Thr kinase activity and are then transported into the cell by nonSMAD / SMAD proteins and then activated by transcription factors in the nucleus. They cause the expression of the target gene. This pathway plays an inhibitory role in the early stages of tumorigenesis with cytostasis and apoptosis, but as cancer cell survival continues, the expression of TGF-b by cancer cells is out of control and increases growth rate, angiogenesis, and metastasis.

Methods: To obtain specialized information and data extraction by entering selected keywords in search engines google scholar, Pubmed, science direct, and NCBI, search and apply filters including full text, abstract and view articles and research documents And we reviewed such as clinical trials, experiments, meta-analyses, systematic reviews, narratives, and case reports, and on the other hand, our priority was on the period 2010 to 2020.

Results: finally, our findings from these researches were that TGF-b signaling controls a very wide and diverse set of cellular processes such as proliferation, detection, differentiation, and adaptation in different species. several factors such as PH, ROS. are effective in activating it. SMADs are a large family of TGF-b signaling pathways that play a large role in this pathway. cooperation between the SMAD and non-SMAD pathways determines the result of the cellular response to TGF-b. the interaction between SMAD and other signaling proteins controls the expression of the target gene at different levels. this paper emphasizes the mechanism of TGF-b signaling along the SMAD and non-SMAD pathways and the importance of mutations in functional components of the TGF-b family. although sometimes mutations in these proteins may occur and disrupt the TGF-b signaling pathway, eventually leading to a variety of cancers.

Conclusion: the purpose of this paper was to investigate the TGF-b pathway in the SMAD and non-SMAD branches. SMAD proteins are expressed everywhere and in all adult tissues of the body. in this article, we discussed the types of SMAD proteins and their functions, which included R-SMAD, CO-SMAD, and I-SMAD. R-SMAD included SMAD1, SMAD2, SMAD3, SMAD5, and SMAD8 which sometimes use SMAD9 instead of SMAD8, CO-SMAD contained only SMAD4, and I-SMAD is divided into two subgroups SMAD6 and SMAD7. among the type of SMADs, only R-SMADs are phosphorylated and activated directly by type 1 kinases. non-SMAD paths are several conditions such as the presence of type 2, TGF-b receptors in the lipid complex. mutations in the TGF-b pathway lead to a variety of spectra of SMAD2 and SMAD3 were high similar to the mutation spectrum of SMAD4 both in mutation type and location.

Keywords: TGF-b signaling pathway, SMAD pathway, non-SMAD pathway, cancer, mutation

Oxidant/antioxidant balance in breast milk: its correlation with maternal dietary patterns and psychological performance (Research Paper)

Samira Karbasi,[1,*] Asghar zarban,[2] Afsane Bahrami,[3]

1. 1Student Research Committee, Birjand University of Medical Sciences, Birjand, Iran
2. 3Department of Biochemistry, Faculty of Medicine, Birjand University of Medical Sciences, Birjand, Iran
3. Cellular and Molecular Research Center, Birjand University of Medical Sciences, Birjand, Iran

Introduction: Human milk composition is dynamic and can depending on various maternal variables like as psychological structure, diet and nutritional condition. Improving these nutrition practices during gestation and breastfeeding is critical for enhancing health outcomes for both mothers and infants. The aim of this study was to investigate the association between oxidant/antioxidant balance in breastfeeding mothers with dietary patterns (DPs) identified using principal component analysis (PCA), and psychological performance.

Methods: Milk samples were collected from 700 mothers, who were selected from 4 different regions through a random cluster sampling. Total antioxidant status (TAS) of milk samples were assessed using ferric reducing/antioxidant power assay (FRAP), 1, 1-diphenyl-2-picrylhydrazyl (DPPH) radicals, malondialdehyde (MDA) and thiol assay. The milk total concentrations of total protein, calcium (Ca) and triglyceride were estimated with using commercial kits. A validated food frequency questionnaire (FFQ) that comprised 65 food items and this was used to determine major dietary patterns in this group, using PCA. Depression, anxiety, quality of life (QL), general health (GH) and cognitive ability were obtained using reliable and valid questionnaires.

Results: Two major DPs were identified: “healthy” and “unhealthy”. The healthy pattern was characterized by a high intake of vegetables, fruits, fish, low fat dairy products, whole grains and nuts and the unhealthy pattern, was determined by high intake of sweetened sugary beverage, high-cholesterol diet, red meats, poultry, processed meats, sweets. Subjects with highest tertile of healthy DP had higher scores of milk DPPH and thiol, compared to those first tertile healthy DP ($p<0.05$). Milk Ca and thiol was significantly lower in the third tertile of unhealthy DP versus the first tertile ($P<0.05$). Mothers in the healthy DP group had significantly higher cognitive ability, QL scores compared to unhealthy DP group (P value <0.05). On the other hand, anxiety, depression and total GH were positively linked by the unhealthy DP and inversely linked by the healthy DP (P value <0.05).

Conclusion: Our findings show which adherence to a healthy DP identified with high consumption of vegetables, fruits, fish, low fat dairy products, and whole grains is linked to a higher milk oxidant/antioxidant status and lower possibility of psychological disorders in Iranian mothers.

Keywords: Oxidant/antioxidant balance, dietary pattern, breastfeeding mothers, psychological performance

Oxidative Stress and Pathogenesis of Breast Cancer (Review)

ali esnaashari,[1,*] faeze ghazanfaripoor,[2]

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Introduction: Reactive oxygen and nitrogen species (RONS) are produced by several endogenous and exogenous processes, and their negative effects are neutralized by antioxidant defenses. Oxidative stress (OS) occurs from the imbalance between RONS production and these antioxidant defenses. Previous studies indicate the important roles of oxidative stress in different tumour pathogenesis including colorectal, bladder, endometrial carcinoma and breast cancer. Breast carcinoma is one of the most common neoplasms in women and is a leading cause of cancer-related deaths worldwide. We conducted this review to summarize the most recent published literature on oxidative stress biomarkers and breast cancer.

Methods: A review literature search of eligible studies was conducted in PubMed database from 2010 to 2021 for studies evaluating the association between oxidative stress and breast cancer using the following search strategy: ("oxidative stress" OR "RONS") AND ("breast carcinoma" or "breast cancer") as keywords. Studies (systematic review and metanalysis) were included in this review.

Results: Studies suggest that in this disease oxidative stress is increased. Many mechanisms are effective in enhancing oxidative stress, including genetic variations in antioxidant enzymes, estrogen therapy, and excess reactive oxygen species. It has been shown that breast carcinoma DNA contains high concentrations of base modifications. An increased level of 8-hydroxy-2′-deoxyguanosine (8-OHdG) was observed in estrogen receptor (ER) positive malignant tissues which suggests that ROS may play an important role in the early phases of carcinogenesis. Moreover, increased ROS has been found in the tumor environment that plays an important role in cancer progression by altering the expression of suppressor genes involved in apoptosis, increasing the expression of cytokines involved in angiogenesis, creates changes in the connections between cells and their effects on the metalloproteinase activity of proteinase involved in metastasis.

Conclusion: Destruction caused by oxidative stress has an impressive role in the occurrence and progression of breast cancer. In other words, an increase in cell proliferation leading to tumor mass requires a constant blood supply. Hypoxic tumor cells are affected. Hypoxia leads to increased free radicals, stimulates the expression of HIF-1α, VEGF expression, and angiogenesis in

the tumor environment. Furthermore, increased ROS leads to a reduction in intercellular adhesion and the activation of metalloproteinases involved in metastasis. This process facilitates the migration of cancer cells to other parts of the body. Thus, increases in free radicals and oxidative stress both play important roles in the development of cancer.

Keywords: Reactive oxygen and nitrogen species, antioxidant defenses, Oxidative stress.

Pathogenesis of Preeclampsia: Role of Oxidative Stress (Review)

Parastoo Ravanbod,[1,*]

1. Bousheehr university of medical sciences

Introduction: Preeclampsia (PE) is a major disease of human pregnancy, marked by hypertension and proteinuria, appearing during the second or third trimester of gestation. Incidence differs depending on geographical region, time of year, nutrition, and race/ethnicity, but it affects roughly 3–8% of women worldwide. The mechanisms responsible for the pathogenesis of preeclampsia are unclear. It has been reported that preeclampsia is associated with endothelial dysfunction, systemic vasoconstriction, inflammation, oxidative stress, and intrauterine growth restriction, and multiorgan dysfunction. Reactive oxygen species (ROS) are highly reactive free radicals, including superoxide (O−2), hydrogen peroxide (H2O2), hydroxyl radical (OH), and peroxynitrite (ONOO−) that damage protein, DNA, and RNA within a cell causing cellular dysfunction and death. Oxidative stress is created by the imbalance between ROS and antioxidant defense of the cell. During normal gestation, ROS production is reported to be increased; however, excessive ROS production has been reported in pathological states, such as preeclampsia. In this article we will review studies evaluating the role of oxidative stress in terms of pathogenesis of preeclampsia.

Methods: In order to find relevant studies to the research question, an electronic search with time (recent five years, up to 2021) and language (English) restrictions was conducted using PubMed including “Preeclampsia”, “Oxidative stress” and “Reactive Oxygen Species” keywords. Most recent studies including case control studies, original research and review articles were selected. Analysis was done and data were synthesized and compiled in a sequential and presentable paradigm.

Results: Several studies relate the development of preeclampsia with the inadequate invasion of the trophoblast and uterine artery remodeling due to the abnormal regulation of cell–cell and cell–matrix interaction. In preeclamptic women, maternal circulating levels, placental tissue levels and production rate of lipid peroxides are increased, and several antioxidants are markedly decreased. One study suggested the role of SOD3 single nucleotide gene polymorphism in the increased oxidative stress in preeclampsia. A significant decrease in tissue levels of vitamin E, and in the activities of superoxide dismutase and glutathione peroxidase are found in the placenta of these women. Another source of oxidative stress in preeclamptic women is the activation of leukocytes in their circulation which has been reported by several articles. It has been also stablished that in preeclampsia, maternal circulating neutrophils and monocytes are activated, which generate

superoxides (O2) by the activity of NADPH oxidase and hence cause oxidative stress. Plasma thrombomodulin, an anticoagulation factor, is also significantly elevated in women with preeclampsia, with elevations detected as early as 24 weeks into the pregnancy.

Conclusion: The available literature reveals that Preeclampsia is characterized by increased oxidative stress due to the imbalance between lipid peroxidation and antioxidant defense mechanisms, leading to endothelial dysfunction and free radical mediated cell injury. A comprehensive understanding and the detailed knowledge of the pathogenesis of the preeclampsia will enable us to identify the responsible contributing bio-molecules for this disease. Measurement of these contributing biomolecules can help us in predicting the disease earlier. It is hoped that we can identify the biomarkers of preeclampsia with high predictive, preventive, and prognostic value and incorporate with current clinical practice to improve the care for pregnant women.

Keywords: Preeclampsia, Oxidative stress, Reactive Oxygen Species, Antioxidant Defense

PCR and cloning of the lcs chimeric gene in pcDNA3.1 vector and its expression in the cell line (Research Paper)

Sepideh Saroughi,[1,*] Maryam Zare,[2] Rouhollah Kazemi,[3] Mohammad-Javad Motamedi,[4] Jafar Amani,[5]

1. BMI Hospital
2. Dept. of Biology
3. PhD in Molecular Genetics
4. PhD in Molecular Genetics
5. Chemical Injuries Research Center

Introduction: Diarrhea is the second most common cause of under-5 mortality. The most important strains of Entrotoxigenic Escherichia coli causing Lt and St toxin cause diarrhea and Entrohemoragic E.coli causing Shiga-like toxin secretion. Chlorine enterotoxin B subunit (Ctx) plays a key role in the development of diarrhea in Vibrio cholerae. More specific antibodies could be developed to counter these toxins by combining the CtxB, LtB and StB (LSC) epitopes and the production of trivalent vaccine. The aim of this study was to cloning lsc gene into pcDNA3.1 to design a vaccine DNA.

Methods: The lsc gene sequence was transferred to pcDNA3.1(+) vector after primer design and amplification by PCR. The pcDNA3.1(+) vector and the PCR product were digested using HindIII and EcoRI enzymes. Cloning of lsc gene was performed in pcDNA3.1(+) vector and PCR. The clones were digested enzymatically. To ensure expression of lsc gene, it was transferred to HEK-293T cell and confirmed by Western blotting

Results: The lsc gene was confirmed by PCR and cloning in pcDNA3.1(+) vector using enzymatic digestion and a fragment length of 933 bp was detected and confirmed. Transfection kit was then transferred to HEK-293T cell and expression of the recombinant protein was confirmed by Western blotting and the protein was 39 kDa.

Conclusion: The results of the chimeric gene are well expressed in the cell line and confirmed by Western blotting that can be a good candidate for the fight against bacterial infection.

Keywords: Cloning, lsc gene, DNA vaccine

Perfusion Bioreactors for Tissue Engineering (Review)

Soheil Kianirad,[1,*] Zahra-Beagom Mokhtari-Hosseini,[2] Ashrafalsadat Hatamian-Zarmi,[3] Mohammad Naji,[4] Elham Ansari,[5] Zahra Kazemizadeh,[6]

1. Department of Life Sciences Engineering, Faculty of New Sciences and Technologies, University of Tehran
2. Department of Chemical Engineering, Faculty of Petroleum & Petrochemical Engineering, Hakim Sabzevari University
3. Department of Life Sciences Engineering, Faculty of New Sciences and Technologies, University of Tehran
4. Urology and Nephrology Research Center, Shahid Beheshti University of Medical Sciences
5. Department of Life Sciences Engineering, Faculty of New Sciences and Technologies, University of Tehran
6. Department of Chemical Engineering, Faculty of Petroleum & Petrochemical Engineering, Hakim Sabzevari University

Introduction: Tissue engineering is the regeneration or reconstruction of living and functional tissue to treat injuries or diseases. Its three key components are cells, scaffold, and provision of a culture medium that mimics the physiological conditions to stimulate and cultivate cells. In body, there are mechanical and biochemical interactions between cells and their extracellular matrices. In earlier studies of tissue engineering, static culture medium was used. Disadvantages and limitations of this classical method include inhomogeneity of nutrient concentration, accumulation of waste materials, lack of mechanical signals in culture medium and inefficiency in the production of three-dimensional tissues. A bioreactor was used to overcome the limitations and create a dynamic culture medium for cells. Bioreactors are commonly used in tissue engineering and include a variety of types such as perfusion, Spinner flask, rotating wall vessel, hollow fiber membrane, mechanical stimulation and biaxial rotating. One of the most similar bioreactors to the natural conditions of the body are perfusion bioreactors. In the past, the transfer of cell suspension to scaffold pores was done manually, relying on the force of gravity. In 3D scaffolds, the force of gravity alone cannot transfer cells and nutrients into the pores of the scaffold. The best available approach that results in uniform and effective cell seeding in scaffolds is the perfusion method.

Methods: In this review, information collected from articles related to perfusion bioreactors and their simulation and modeling were used to provide a summary of their recent advances, applications, Advantages, and limitations.

Results: Bioreactors in tissue engineering mimic the physiological conditions, producing functional tissue to repair or replace damaged tissue. Perfusion bioreactors are one of the most widely used bioreactors in tissue engineering, which by injecting the culture medium into the culture chamber, provide conditions similar to the blood supply to cells through the arteries. In these bioreactors, the continuous flow of culture medium passes through the surface of cells in a pulsating or non-pulsating manner, and the process of absorbing nutrients and removing waste products from cells are similar to the body. Perfusion bioreactors have been used in tissue engineering for various applications. For example, Perfusion bioreactors were used in liver tissue engineering for cell viability enhancement, in adipose tissue engineering by creating hypoxic conditions to increase cell proliferation, and in cartilage tissue engineering by changing the relative pressure of oxygen to produce the cartilage tissue. They were used in bone tissue engineering to increase nitric acid production and bone differentiation of cells by increasing shear stress, and in another study, by applying perfusion and rotational mechanical forces, cell proliferation and increasing in alkaline phosphate enzyme expression were achieved. This bioreactor was utilized in tracheal tissue engineering to investigate the effect of fluid transfer mechanism on wall shear stress and cell seeding. Moreover, with the help of perfusion bioreactor, mechanical stimulation was applied to study cell proliferation in urethral tissue engineering. Also, it was used in ureter tissue engineering to investigate the effect of pulsed mechanical stimulation on cell nutrition and cell orientation. One of the major problems of perfusion systems is the formation of air bubbles in the passage of the fluid, which causes changes in local stress, blockage of the fluid path and increase the local flow rate. Using the bubble trap system, the bubbles created can be removed to some extent. Also, the use of oxygen delivery methods, such as the use of silicone membranes or tubes, reduces the rate of bubble formation in the fluid path.

Conclusion: Perfusion bioreactors are mostly used in tissue engineering due to their uniform distribution of nutrients as well as their ability to create a quasi-physiological environment for cell growth. In perfusion systems, it is possible to continuously control and monitor environmental and operational variables of the process such as component concentration, temperature, pressure and flow rate. These bioreactors increase mass transfer and, by applying shear stress stimuli, provide the physical signals necessary for cell differentiation and proliferation to function optimally. However, cell separation at high flow rates is one of their disadvantages. By optimizing the flow rate and combining forces such as rotation and perfusion, the performance of these bioreactors can be improved.

Keywords: Bioreactor, Perfusion, Tissue engineering, Mass transfer, Computational fluid dynamics

Personalized treatment of COVID-19 disease as a major breakthrough in the quest for a cure (Review)

Neda Golpar raboki,[1,*] Fatemeh Akbarian,[2]

1. Ale-Taha Institute of Higher Education, Tehran, Iran
2. Ale-Taha Institute of Higher Education, Tehran, Iran

Introduction: SARS-CoV-2 is one of the main subfamilies of coronaviruses with four known genera. The virus infection process is through binding to the ACE2 receptor on the cell surface through spike protein. Recently, large databases have been created to sequence and share different types of SARS-CoV-2; they show that some of these variations positively impact infection severity of the virus and the ability to escape from the immune system, leading to its further evolution. Subsequently, the evolution of the virus leads to the creation of new types with an increased level of infection, contagion, and even resistance to existing drugs. For example, SARS-CoV-2 spike P681R mutation transforms a proline residue into an arginine, resulting in a 40% increase in delta-type viral infectivity compared to other types. Therefore, it is necessary to create a platform for classifying the lineages based on their severity of the infection, contagion, etc. This platform should include effective treatments related to each lineage, as well as genetic profiles and medical records of each patient. As the most outstanding example of countries administrating personalized medicine for confronting the pandemics, Andalusia has collected the genetic profiles of its population since 2001 and analyzed the sequences of patients and the virus with the help of artificial intelligence. They discovered the natural history of the virus, the infectious process, response to treatments with antiviral drugs, and the body's response to the vaccination process. Thus, the spread of this disease might be urgently controlled through personalized medicine.

Methods: People are divided into different groups based on their genetic profiles and epigenetic factors to receive treatments and health care in personalized medicine. Thus, not only the quality of health care will increase, but the need for unnecessary tests and the cost of treatment will reduce. Employment of personalized medicine in the health system along with sequencing and categorizing microbiome sequences in different geographical areas mediate early identification of pandemics, such as COVID-19, and their transmission pattern in each region before the massive crisis.

Results: One of the largest databases recently gathered by the efforts of nineteen countries comprises the genomic sequences of patients with severe COVID-19 disease. The most effective variations related to SARS-CoV-2 can be identified utilizing this platform; researchers have found that the variant located at locus 3P21.31 has the highest association with the reproductive

and severity of the infection, and people with this variant are more likely to develop the dangerous phenotype of COVID-19. This locus encodes various proteins that are not directly related to the infectivity of SARS-CoV-2 but may be indirectly influential. For example, ccl is a chemotaxis mediator for circulating monocytes, and its receptor is encoded by ccr9 gene located at this location. Research has shown that in patients with severe coronavirus phenotype, the expression of ccr9 and its ligand increases in monocytes and other body fluids. Therefore, it can be concluded that excessive expression of ccr9 can be one of the reasons for the various rates of inflammatory reactions in different people.

Conclusion: Furthermore, other studies have shown that loss of function in the TLR7 gene located on the X chromosome is strongly associated with the development of the acute SARS-CoV-2 phenotype. This gene plays an essential role in the production mechanism of interferon 1 (IFN1), which is produced by virus-infected cells and prevents propagation of the virus. Therefore, patients with impaired production of IFN1 are not able to fight against coronavirus infection. In addition, the tissue damage, inflammation, and functional disorders that result from infection vary in different hosts. Aside from genetics, epigenetic factors are also involved in developing the acute type of virus. Each individual has different reactions to the disease due to vaccination, conditions they have faced during their life, and the health status of the immune system. In primary infection of some patients, B and T lymphocyte counts rise sharply, while in others, they may not respond at all. Therefore, diagnosing susceptible individuals at risk of exacerbation of disease and acute phenotype can help the health system, in which personalized medicine can play a very effective role. The necessary contexts for personal therapy include the establishment of microarray laboratories, the construction of bioinformatics platforms, the collection of mutation information, and, above all, the introduction of physicians to the concept of genetic profiling. It is crucial to create a strong link between the clinical department and the laboratory so that in case of an outbreak of the disease or discovering a solution for the treatment or control of the disease, the health system will immediately inform. In conclusion, overcoming pandemics such as COVID-19 occurs only by the full cooperation of the clinical sectors, laboratories, and politicians worldwide. Thus, countries will be prepared to face this kind of viral attack in the future.

Keywords: Personalized medicine, COVID-19, SARS-CoV-2, Genetic profiles, Epigenetics

Photodynamic effects of Rose bengal on cancer cells lines (Review)

Parnia Hemmati,[1,*] Seyed Mehdi Tabaie,[2] Mina Sadat Naderi,[3]

1. Department of Cell and Molecular Biology, Faculty of Biological Sciences, Islamic Azad University, Tehran North Branch, Tehran, IRAN
2. Department of Medical Laser, Medical Laser Research Center, Yara Institute, ACECR, Tehran, IRAN
3. Department of Biophysics, Faculty of Biological Sciences, Islamic Azad University, Tehran North Branch, Tehran, IRAN

Introduction: Introduction: Cancer is one of the leading causes of death worldwide. Cancer causes uncontrolled cell division, which can lead to tumors, damage to the immune system, and other fatal disorders. Cancer is recognized as a major cause of death and an important barrier to increasing life expectancy in every country in the world. There are several treatments for cancer. One of these methods is photodynamic therapy (PDT). Photodynamic therapy (PDT) is a promising minimally invasive treatment for cancer that uses non-ionizing radiation (in most cases) and its cytotoxic mechanisms cause limited damage to DNA and connective tissue structures and collagen. This treatment can be used as many times as needed by doctors, something that is not possible with current treatments (surgery, chemotherapy and radiotherapy). PDT does not have a "memory effect" as radiation therapy.This treatment involves the administration of a light-sensitizing agent (PS) and the subsequent stimulation of the PS with laser light at a specific wavelength. The evoked PS then reacts with cellular oxygen and produces reactive oxygen species (ROS)which kill tumor cells by direct and indirect cell death mechanisms. Ps sensitizers are used in various photodynamic therapies. One of these sensitizers is Rose bengal. Bengal rose (4,5,6,7-tetrachloro-2%, 4%, 5%, 7% -tetraiodo-fluorescein disodium or RB) is a known type II light sensitizing agent and thanks to the presence of several chlorine and Iodine on xanthine rings shows easy photocatalytic conversion of triple oxygen. Bengal rose has also been used as a treatment for some cancers and skin diseases. Rose Bengal has also been used as a light sensor in the photodynamic therapy of breast cancer. In this method, laser green light has been used. According to the articles, Rose bengal has also been used as a sensitizer in the treatment of A375 cell line (human melanoma cell line) and direct sunlight has been used instead of laser light. Larynx cancer also uses the Rose bengal sensitizer and green light laser, and the number of cancer cells to the extent Decreased upper.

Methods: Methodology: This literature review was a cross-sectional study by popular search engines in medical sciences include PubMed, Science Direct, Google Scholar, Elsevier, and Scopus over the past 5 years .

Results: Result: Rose bengal medicine can be used to treat some cancers such as skin, breast, larynx as well as skin diseases.

Conclusion: Discussion: According to review studies, it can be concluded that some drugs such as Rose Bengal due to their structural and chemical properties can play a role as a light sensitizer in the treatment of many cancers by photodynamic methods. And this study can be useful in improving treatment methods.

Keywords: PDT, Cancer, Rose Bengal

Phylogenetics, molecular biology and clinical aspects of corona virus (Review)

Negin Motavalizadehkakhky,[1,*] Hadith Nasrabadi,[2] Zahra Kheiri,[3] Mahshid Meshkani,[4] Negar Motavalizadehkakhky,[5]

1. Mohebbi Model School, 10th grade, Neyshabur, Iran
2. Mohebbi Model School, 10th grade, Neyshabur, Iran
3. Mohebbi Model School, Neyshabur, Iran
4. Islamic Azad University, Neyshabur Branch, Neyshabur, Iran
5. Islamic Azad University, Faculty of Pharmacy, Damghan Branch, Damghan, Iran

Introduction: Abstract: Background and Purpose: COVID-19 is a viral respiratory illness. In this paper, we take a look at the Coronavirus genome, the symptoms of coronavirus (COVID-19), coronavirus prevention and treatment as well as different types of COVID-19 vaccines. Materials and methods: the articles were searched looking for keywords including COVID-19, vaccine, treatment, prevention, and genomic structure of the virus. It is worth mentioning that reliable websites and other references are used to obtain information about developing a novel vaccine have been listed and referenced at the end of the article. Results: In late 2019, a new viral disease broke out in China which was named COVID-19 by WHO. Due to the similarity to the virus causing acute respiratory syndrome and SARS virus, it was called Sars-CoV-2. This virus causes a life-threatening lower respiratory tract infection1.

Methods: Materials and methods: the articles were searched looking for keywords including COVID-19, vaccine, treatment, prevention, and genomic structure of the virus. It is worth mentioning that reliable websites and other references are used to obtain information about developing a novel vaccine have been listed and referenced at the end of the article.

Results: Results: In late 2019, a new viral disease broke out in China which was named COVID-19 by WHO. Due to the similarity to the virus causing acute respiratory syndrome and SARS virus, it was called Sars-CoV-2. This virus causes a life-threatening lower respiratory tract infection1.

Conclusion: Conclusion: Coronavirus causes COVID-19 viral disease, affecting a large number of people around the world. In general, virus entry to the host cells is mediated by spike protein (crown-like proteins) and hence it can be taken into account as an appropriate candidate for efficient vaccine design. This protein enters the host cells through human ACE 2 receptors. This receptor has been detected in some organs including the lungs, heart,

liver, kidneys, brain, and bladder, and hence these organs can be severely damaged due to COVID-19 infection6. Antigen-specific antibodies are secreted in response to the coronavirus attack and consequently, the body is protected against virus reattack. Coronavirus mutations do not happen quickly and the virus genome mutates in terms of changes in the amino acid structures. This change may occur due to nucleotide addition or deletion from the viral genome. To prevent the disease before applying an efficient vaccine, people should follow the recommended instructions and observe personal proper hygiene to keep themselves, their families, and their community healthy and visit a doctor in the presence of any symptoms or clinical manifestations. Investigations on the efficiency of various available vaccines reveal that the killed viruses in a vaccine function more efficiently compared with a membrane protein. Because the membrane protein should be combined with a non-pathogenic virus like adenovirus-based vectors and this virus may be deactivated by the human body immune system and consequently, its efficiency decreases. Innovation: Coronavirus can introduce to the human body through one of the viruses which people are vaccinated against it in childhood, so it can stimulate immune system response and consequently releasing coronavirus antigen-specific antibodies. This sequence of events leads to virus destruction and prevents COVID-19 development. Surveys demonstrate that compared with using viral proteins, using killed viruses provide more effective immunity, as they are resistant to all mutations. We hold this view that applying combination of the killed virus vaccine like smallpox (because smallpox is a viral disease which can be transmitted through cows to humans as an intermediate host, while cows themselves are not affected by the virus and our immune system knows the smallpox virus from our childhood because we have vaccinated for smallpox virus) with killed coronavirus (a new virus for our immune system) is more efficiently in comparison with other types of available vaccines. It can be explained that since there is an immunologic memory against smallpox in the human body, the immune system initially identifies smallpox and then the coronavirus genome within. After that, specific antibodies against the smallpox virus are released and then there is a high possibility of trapping the virus compared with using other viruses. This approach has a lot of advantages. For instance, in the USA, in nursing homes, where the elderly received Pfizer vaccine, several deaths were reported. It can be explained by this fact that the immune system of these people is not strong enough to fight against the virus and are weaker compared with the other age groups of people. These deaths may have happened due to the formation of a blood clot. So, by taking the advantage of this approach, we provide a guide for white cells to fight against the virus rapidly and maybe prevent clot formation in the elderly people. It is recommended to receive medication in the second and third phases through nasal injection because COVID-19 is a respiratory disease and macrophages inside the lungs as phagocytes can destroy the virus easily and prevent developing respiratory disease. It should be noted

that sometimes this approach does not work. However, even if this theory is rejected, these viruses can still stimulate antibody production and develop resistance to the virus but how? That is the question. Firstly, a new virus may develop which cannot be recognized by the human immune system, so there is no memory. Yes, that is possible. However, this vaccine contains killed viruses so it is safe and harmless. Secondly, the human body produces antibodies even against these viruses and it will has a function like previously developed vaccines like sputnik V and stimulate immunity in the human body. Introduction: In late 2019, a case of pneumonia of unknown etiology was reported in Wuhan City. This pneumonia caused symptoms including dry cough, fever, shortness of breath, and acute respiratory syndrome. The clinical symptoms of patients were similar to phylogenic of the coronavirus and therefore, WHO named it COVID-19. This virus belongs to the Betacoronavirus family (HCOV-OC43, HCoV-MERS) 2, and like its other relatives, is capable of infecting a wide variety of organisms serving as intermediate or final hosts. The genome sequence of coronavirus is 88% similar to the two Betacoronavirus types of acute respiratory syndrome-like diseases and 50% similar to the genomic sequence of Mers-CoV. Genomic analysis of this virus reveales the homology with bat coronaviruses or SARS genomes, implying the possibility of COVID-19 transmission from bat to human. This article elucidates biology, genomic structure, ways of transmission, the symptoms of coronavirus infection, prevention, and treatment, comparison of available vaccines, and eventually the mechanism underlying the action. Coronavirus biology: coronavirus is referred to as a group of viruses. The term "Corona" means crown which refers to the appearance of the virus under a microscope. This virus has a fringe of large, bulbous surface projections and looks like a royal crown3. Coronaviruses are a large family and give rise to asymptomatic common colds. They affect the lungs and cause acute respiratory diseases like SARS. In February 2020, the International Committee on Taxonomy of Viruses (ICTV) called it Severe Acute Respiratory Syndrome Type 2. Over the past two decades, corona caused three acute respiratory epidemics namely null corona, severe acute respiratory syndrome (SARS), and Middle East Respiratory Syndrome (MERS)1. The members of the corona family have capsids and their genetic material is a single-stranded positive ribonucleotide4. On the capsid, there are glycoprotein structures called spikes (rod-shaped)1. Other protein compounds are also found on the capsid and protein envelope of coronaviruses' genetic material. The type and structure of these compounds stimulate human immune system response, and that is why they are called viral antigens5. Angiotensin-converting enzyme 2 (ACE2) receptors mediate Severe Acute Respiratory Syndrome Type 2 entrance to the host cells. Virus binding to ACE 2 receptors plays a crucial role in infecting human lung cells and associated pathogenicity6. This virus has presumably originated from bats and has been adapted to infect human cells. Virus directly enters host cells through membrane fusion and then endocytosis. After that, genetic material is

released into the cytoplasm. Initially, glycoprotein components of the capsids are made and these components enter to the Golgi apparatus and endoplasmic reticulum. Released by budding as small vesicles from the intracellular membranes, new mature virus particles are fused with the host cell membrane, and finally, surrounded by host cell-derived lipid membranes are released1,7. Coronavirus genome: As an RNA virus, the Corona genome consists of a helical or circular nucleocapsid. This virus codes replicase as an enzyme that consequently produces new transcripts. As the virus enters host cells, the viral genome is replicated and the virus starts amplification. Sometimes, an error occurs that changes the RNA sequence. These changes are known as mutations8. Coronaviruses are genetically divided into 4 groups including alpha, beta, gamma, and delta. Alpha and beta infect mammalians, while gamma and delta infect birds. SARS and MERS are highly pathogenic and are transmitted to humans through Civet and camel respectively. Coronavirus genome size ranges from 26000 to 32000 base pairs and can have a varied number of open reading frames between 6 and 11. 67% of ORFs code non-structural proteins and 33% code structural and helper proteins. The structural glycoproteins include: A) spike protein (S) B) small envelope protein (E) C) matrix protein (M) and D) nucleocapsid protein (N)2. The symptoms of coronavirus (COVID-19): the most common symptoms of coronavirus are as follows: cough, tiredness, fever, runny nose or nasal congestion, headache, gastrointestinal symptoms like nausea and vomiting, loss of sense of smell or taste. Moreover, in severe cases respiratory problems, shortness of breath, lung infection and kidney failure are also observed. The associated symptoms are divided into 4 groups: a) asymptomatic b) the onset of symptoms: fever lower than 38 °C, sore throat without nonproductive cough, smell or taste loss, nausea, vomiting, anorexia, diarrhea, muscle aches, and tiredness c) stage 2 (respiratory stage): intermediate: more severe symptoms, gastrointestinal and neurological symptoms, shortness of breath, feeling of pressure and pain on the chest with no fever. In the second stage, the involvement of three or four pulmonary lobes at most with an area involvement of less than one-third of each lobe or one or two lobes with a larger area is also observed. D) Severe: affecting over 50 percent of the lungs. Laboratory findings: elevated liver enzymes or triglycerides, organ failure, increased or decreased platelets, slightly elevated troponin levels, and low eosinophil count2. Coronavirus prevention: Wearing face masks by patients and others, frequent hand washing, avoiding close contact with patients, etc. is highly recommended2. Different types of COVID-19 vaccines: 1. Initially developed in Russia, Sputnik V was the first vaccine produced against coronavirus worldwide. In this vaccine, coronavirus along with two other manipulated types enter the host cells. The vaccine makes the host cells copy the horny protein of the virus to stimulate the immune system to produce antigen-specific antibodies against wild-type viruses9, 10. 2. Non-replicating vectors vaccines including Oxford/AstraZeneca vaccine (Sweden-England), Gamaleya (Russia), and Johnson & Johnson (the USA). In this

vaccine, a segment of the viral genome that codes for viral spike antigen is selected. This segment is changed so that spike protein is fixed on the cell surface. Gene expression is regulated by a designed specific promoter. This segment is inserted into a harmless carrier (vector) like adenoviruses which are unable to replicate6. 3. Vaccines contain Killed pathogens such as shafapharmed (Iran) and Sinopharm (China): in this type of vaccine, viruses are firstly cultured in standard cells and then deactivate by chemicals such as β-Propiolactone or gamma radiation so that their structure is preserved. Compared with the vectors, they are easier to produce, have a longer shelf life, have higher stability if kept refrigerated, do not replicate in the body, and last but not least, stimulate to produce good neutralizing antibodies6, 11-13.

Keywords: Corona virus, Acute respiratory syndrome, Virus genetic mutation, Vaccine, Corona treatment

Physician Burnout: a Brief Review of Its Definition, Causes, and Consequences (Review)

Mina Akbarirad,[1,*] Mehdi Hassanzade Daloee ,[2] Mehrdad Sarabi ,[3]

1. Department of Internal Medicine, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. Cardiovascular Research Center, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
3. Medical student, Student Research Committee, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Introduction: Burnout among physicians is a potential warning to the health system and one of the prime occupational hazards of recent years. Burnout is characterized by emotional, mental, and physical fatigue. Numerous studies have shown that burnout has a high prevalence among physicians, such that about one-third of them are affected at some point in their career. A recent study from the United States reported that 45.8% of physicians present at least one symptom of burnout. Statistics indicating one suicide per day among physicians show the urgency of the matter and the need for improvement. It has been reported that this syndrome may even start from the beginning of medical studies such that medical students and r=is review article, we describe the main cause and consequences of physician burnout.

Methods: To investigate the issue, the two keywords of “burnout” and “physician” were searched in PubMed, Medline, Sciences Direct, and Google Scholar. We did a comprehensive literature review to extract any recent related content about the cause and consequences of physician burnout.

Results: Drawing from the studied literature, it is concluded that to address the issue, first, the elements of physicians’ wellness and satisfaction should precisely be determined, then necessary interventions should be adopted to improve the situation.

Conclusion: Drawing from the studied literature, it is concluded that to address the issue, first, the elements of physicians’ wellness and satisfaction should precisely be determined, then necessary interventions should be adopted to improve the situation.

Keywords: Burnout Depression Physician Suicide

Phytotherapy in Idiopathic Heavy Menstrual Bleeding: A Systematic Review (Review)

Mohammad Amin Talebpour,[1] Minoo Momenzadeh,[2,*] Amir Hussein Bueik,[3]

1. Student Research Committee, Islamic Azad University, Mashhad branch, Mashhad, Iran.
2. School of Medicine , Mashhad Islamic Azad University, Mashhad , Iran
3. Student Research Committee, Islamic Azad University, Mashhad branch, Mashhad, Iran.

Introduction: Background: Idiopathic heavy menstrual bleeding (HMB; IHMB) is a common gynecological problem with no pelvic pathology or general bleeding disorder. Herbal remedies are commonly used to treat HMB. This systematic review aimed to assess the effectiveness and safety of herbal preparations for the treatment of IHMB.

Methods: Methods and Search strategy: MEDLINE, Ovid, and the Cochrane Central Register of Controlled Trials were searched from 2010 to 2020 December. Only randomized controlled trials were considered.

Results: Results: Eight randomized controlled trials were included in this systematic review. Different herbal preparations were used in the included trials. In four studies, Ginger capsules and myrtle fruit syrup significantly reduced the menstrual duration and blood loss compared with placebo based on the pictorial blood loss assessment chart score ($p < 0.001$, $p = 0.01$). In other trials, Punica granatum flower capsules were as effective as tranexamic acid capsules in reducing the mean (SD) pictorial blood loss assessment chart score, with no significant difference between the two treatments ($p = 0.3$).

Conclusion: Conclusion: The results show that the methods used in these trials may reduce menstrual bleeding in women with IHMB. Additional well-designed trials are needed to investigate the safety and efficacy of herbs for the treatment of women with IHMB or other forms of HMB.

Keywords: Keywords: menorrhagia, idiopathic heavy menstrual bleeding, herbal medicine.

Platelet Generation Using Stem Cell Technology (Review)

Reyhaneh Abriyan,[1] Amir Atashi,[2,*]

1. Student Research Committee, Shahroud University of Medical Sciences, Shahroud, Iran
2. Stem Cell and Tissue Engineering Research Center, Shahroud University of Medical Sciecnes, Shahroud, Iran

Introduction: Platelet transfusion is a lifesaving procedure that is done to prevent bleeding or stop ongoing bleeding which is occurred in patients with low platelet or impaired functional platelet. Platelet is a scarce resource as its processing requires a great deal of precision to assure its quality. Recent advances in platelet transfusion research have been very significant. The most important of these advances has been in creating independent platelet donor production of platelets using stem cell technology. Using this technology, platelets can be generated that is sufficiently sure of the absence of the pathogens and also platelets antigens, especially HLA. Perhaps the most important achievement of this technology is the prevention of platelet refractory, which is commonly seen among patients receiving allogeneic platelet transfusion.

Methods: To produce platelets, c-MYC, BMI1, and BCL-XL genes are first transduced into megakaryocytes differentiated from induced Pluripotent Stem Cells (iPSCs). By doing this, the megakaryocytes turn into immortal cells (imMKCLs). Researchers have also been able to provide free feeder culture conditions for imMKCLs using drug combinations. Then, by placing these cells in a special bioreactor that has turbulent flows and under the influence of soluble factors such as macrophage migration inhibitory factor, insulin growth factor binding protein 2, and nardilysin secreted from imMKCLs, the process of thrombopoiesis is completed.

Results: The important point here is that researchers succeeded to experimentally transfused platelets produced in the above method into a patient with alloimmune platelet transfusion refractoriness.

Conclusion: This technology has made it possible to produce platelets in large quantities, safely and without dependence on donors. Certainly, with the introduction of these platelets into blood transfusion medicine, we will see a significant change in the field of platelet transfusion.

Keywords: Platelet, induced Pluripotent Stem Cell , megakaryocyte

Point Mutation Effect on Diphtheria Toxin- based Immunotoxin against Granulocyte-Colony Stimulating Factor Receptor In silico as Targeted Therapeutic Strategy (Research Paper)

Ghazale Faridfar,[1] Mehdi Zeinoddini,[2,*] Shadi Jabbarzadeh,[3]

1. Department of Bioscience and Biotechnology, Malek Ashtar University of Technology, Tehran, Iran
2. Department of Bioscience and Biotechnology, Malek Ashtar University of Technology, Tehran, Iran
3. Department of veterinary medicine ,Azad Islamic University of Karaj, Karaj, Iran

Introduction: Recent advances in the design and administration of immunotoxins are currently in clinical development. Immunotoxin drugs delivery is a non-invasive treatment that inserts from specific receptors on the surface of cancer cells and eliminates them purposefully. These recombinant proteins carry a toxin fused to a targeting cell. Following the ligand-receptor binding of the target cells, the toxin invades the cytoplasm and destroys them. An important feature of the recombinant protein is its ability to isolate ligands from the predictable catalytic domain. Hence, bacteriotherapy development knowledge of cancer has been regarded as a novel and effective technique. Accordingly, Diphtheria Toxin (DT) is broadly applied due to its easy expression, high activity, and minimal side effects for therapeutic. In this initial analysis, we have provided insight into the structural and functional properties of fusion DT387GCSF protein and its receptor. Accordingly, DT387GCSF immunotoxin was contained two portions: truncated diphtheria toxin (DT) and granulocyte-colony stimulating factor (G-CSF). In this study, we first focus on the structure and function of the fusion protein of diphtheria immunotoxin, then we will prepare for further processes. Our study aimed to develop recombinant DT387GCSF protein and evaluate its structural and functional characteristics relative to its receptor.

Methods: According to the scheme objective, the DT387GCSF sequence and its receptor were downloaded in the FASTA format. Following, the three-dimensional structure of the protein was predicted through the DE NOVO MODELING method using the ITASSER server (https://zhanglab.ccmb.med.umich.edu/I-TASSER/). Next, refinement of the predicted models was obtained for efficient structure using 3D refine server. To validate the presented models, the files obtained were evaluated using the server http://molprobity.biochem.duke.edu/. It should be noted the energy level of all PDB files was diminished to the most stable situation using SPDBV_4.10_PC software. The proteins geometry quality was also evaluated based on the Ramachandran plot using the RAMPAGE server (https://servicesn.mbi.ucla.edu/SAVES/). The structure modeling was created

point mutations (C387S) using Molegro Virtual Docker software. Finally, protein-protein interaction was investigated using the Zdock server (http://zdock.umassmed.edu/) and HEX software. Ultimately, the tendency to connect the mutant with the native ligand was compared by the available servers.

Results: The Comparison of binding energy in the native and Ser-387 Mutant samples with their receptor demonstrated no significant difference in the binding affinity of the ligand at their receptor. The outcome also indicated that point mutation improved the accurate functional structure. Generally, the software analysis also explained there was no meaningful distinction in an efficient connection of the mutant protein and its receptor compared to the prime model.

Conclusion: Unlike sulfhydryl (SH-groups) side chains of cysteine, the results demonstrated that the point mutation (ser-387 mutant) doesn't impair the receptor-ligand interaction. Moreover, this process also increases drug production and efficiency. We concluded that DT387GCSF might be useful as a targeted toxin in G-CSF responsive cells. Besides, this review may provide an advantage to gene-based DT therapeutics and novel therapeutic applications in prospect.

Keywords: Diphtheria Toxin, Immunotoxin, GCSF, GCSF Receptor, Protein Modeling, Fusion Protein.

Polycystic ovary syndrome pathogenesis: Potential role of Oxidative stress (Review)

Mahshad Zare,[1,*]

1. Midwifery department, Hafez Hospital, Shiraz, Iran

Introduction: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among women of reproductive age which has been associated with impaired fertility and negatively affects various health systems. Despite a long history of studies on PCOS, its etiology is still unknown. Studies have shown oxidative stress plays a central role in the pathophysiology of many different disorders, including PCOS. Reactive oxygen and nitrogen species (RONS) are produced by several endogenous and exogenous processes, and their negative effects are neutralized by antioxidant defenses. Oxidative stress (OS) occurs from the imbalance between RONS production and these antioxidant defenses. This article reviews the literature data related to the mechanisms of oxidative stress in PCOS.

Methods: In order to find relevant studies to the research question, an electronic search with time (recent five years, up to 2021) and language (English) restrictions was conducted using PubMed. The search terms included “Polycystic ovary syndrome,” “PCOS,” “Reactive oxygen species (ROS),” “Oxidative marker,” “Oxidative stress (OS),” “Antioxidant were used individually or/and in various combinations to retrieve the relevant literatures. Most recent studies including case control studies, original research and review articles were selected.

Results: For investigation of the oxidative stress role in the pathogenesis of diseases, mainly, studies have examined oxidative stress biomarkers including malondialdehyde (MDA) and Nitric oxide (NO) also anti-oxidative biomarkers such as Total antioxidant capacity (TAC). Results of these studies showed higher level of MDA, NO, Advanced glycosylated end products (AGEs) and Xanthine Oxidase (XO) in PCOS women. One meta-analysis showed that there was no significant difference in TAC in women with PCOS compared with control, however in two original studies higher and lower level of TAC was reported.

Conclusion: The association between oxidative stress and PCOS is an important issue in human reproductive medicine. In general, an association between oxidative stress and PCOS has been established in different studies. However, conflicts still exist. Results of studies about antioxidant

concentration are conflicting; therefore, further studies of oxidative stress in PCOS are needed to clarify the association PCOS with antioxidants.

Keywords: Polycystic ovary syndrome, Oxidative stress, Reactive oxygen and nitrogen species, Antioxidant.

POLYCYSTIC OVARY SYNDROME, ORAL DISEASE AND INFERTILITY (Review)

Elham Zare,[1,*]

1. Boroujerd Islamic Azad University

Introduction: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among women of reproductive age which has been associated with impaired fertility and negatively affects various health systems. Studies showed that women with PCOS have increased levels of pro-inflammatory cytokines, groups of proteins that help regulate immunity and inflammation. This chronic inflammation can lead to several oral health problems. The aim of this study was to evaluate the association between oral disease and PCOS.

Methods: In order to find relevant studies to the research question, an electronic search with time (recent five years, up to 2021) and language (English) restrictions was conducted using PubMed. Most recent studies including case control studies, original research and review articles were selected. Analysis was done and data were synthesized and compiled in a sequential and presentable paradigm.

Results: Several studies reported a strong association between periodontal disease and PCOS with a high level of systemic inflammatory markers, including adhesion molecules, TNF-α, IL-1β, IL-6 and monocyte chemoattractant protein. In a cross-sectional study is found that serum C-reactive protein levels were higher in females with newly diagnosed PCOS.

Conclusion: From the mentioned results, there seems to be a positive relation between oral disease and PCOS. However, multicenter studies, with larger sample sizes, are to be conducted to establish a clearer and stronger association.

Keywords: Infertility, Polycystic ovary syndrome, Oral disease.

Polymers used in urethra tissue engineering scaffolds (Review)

zahra kazemizadeh,[1,*] Zahra-begom Mokhtari-Hossini,[2] Mohammad Naji,[3] Ashrafalsadat Hatamian,[4] Sohil Kianirad,[5] Elham Ansari,[6]

1. Hakim Sabzevari University
2. Hakim Sabzevari University
3. Kidney and urethra Diseases Research Center of Shahid Beheshti University of Medical Sciences
4.
5. University of Tehran, Faculty of Modern Sciences and Technologies
6. University of Tehran, Faculty of Modern Sciences and Technologies

Introduction: The main goal in tissue engineering is to design and create a structure similar to the natural structure of a tissue in a living organism, in order to repair tissue damage and lesions. The urethra, as one of the main organs in the urinary system, is an elastic, hollow tube with an inner wall lined with urethral cells that directs urine out of the bladder. urethra diseases can be caused by early conditions such as cancer, fistulas and congenital problems such as hypospadias and epispadias or swelling, infection, injury and injuries caused by surgery. One of the most common urinary tract problems is urethral stricture. More than 300 methods have been proposed and used to treat this disease, but in most of these methods, the reversibility of duct stenosis is very high. In recent years, rapid advances in tissue engineering and regenerative medicine have created a new approach to urethral reconstruction and have offered promising treatment options. In this method, an alternative tissue with the same function as the original tissue is prepared in vitro or in vivo. Polymers play an important role in tissue engineering as scaffolds, and as biological materials, they can mimic the extracellular matrix (ECM) and improve the biological behavior of cells. Scaffolds are made using natural and synthetic polymers that are biocompatible and biodegradable for urethra tissue engineering applications. Polymer selection for designing of scaffold is very important in urethra tissue engineering. Scaffolding should be able to control and mimic the structure and function of urethral tissue. The polymer used, in addition to biocompatibility and biodegradability, must also have the properties of a natural, elastic and impermeable duct to urine. Polymers used in urethra tissue engineering studies can be divided into two groups: synthetic and natural. Synthetic polymers used in tissue engineering must be compatible with the body, degradable and absorbable, and easily converted to various three-dimensional matrix structures. Natural base polymers can easily interact with biological systems and improve cellular behavior such as migration, adhesion, proliferation and differentiation.

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

Results: A wide range of polymer scaffolds have been used to date in tissue engineering. The ideal scaffold should be biocompatible, enhance cell interaction and tissue growth, and have good mechanical and physical properties. The scaffold used to repair the urethra must be impermeable to water to prevent urine from leaking into the growing tissue. In addition, the scaffold needs to be flexible so that the urethra does not become rigid. The advantage of scaffolds containing synthetic polymers is that the structure and mechanical properties and biodegradability can be changed according to the conditions. For example, PGA degraded significantly faster than PLA. Mixing these materials in different proportions produces scaffolds whose destruction different from week to year. One of the disadvantages of these scaffolds is the lack of ECM proteins. Synthetic polymers have better mechanical properties than natural polymers, but if used alone in the scaffolding structure, inflammation and stenosis will occur in the duct. The most important advantage of using natural polymers is that they cause fewer inflammatory reactions. In natural polymers, cell differentiation, signaling and cell adhesion are better but have low mechanical strength, and some, such as collagen and silk fibroin, have high degradation rates.

Conclusion: According to studies and work done in this field, choosing the suitable polymer to regenerate the urethra is still challenging, but it seems that using a combination of polymers with different properties is a more appropriate option.

Keywords: Polymer, scaffold, Tissue Engineering, urethra

Possibility of cultivating Salicornia in the lands of Urmia Lake in order to restore the ecosystem (Review)

Anahita Parsanezhad,[1,*]

1. Farzanegan high school of Tabriz (Sampad)

Introduction: Urmia Lake is a lake in northwestern Iran, which is located between the two provinces of West and East Azerbaijan according to the divisions of Iran and is the sixth saltwater lake in the world. This lake is fed more than Zarrineh, Simineh, Talkheh, Gader, Baranduz, Shahrchai, Nazlu and Zola rivers. It is complete, including the reasons for the dryness of the lake, human reasons such as, construction of highways on the lake, improper use of catchment resources, non-expert agriculture regardless of the area's cultivation capacity, construction of several dams and natural reasons can reduce rainfall Snow and rain and drought were mentioned. According to environmental experts, if the lake dries, the temperate climate of the region will turn into tropical air with salt winds and the environmental conditions of the region will change. In addition to salt, many contaminants, including heavy toxic metals used in agriculture, penetrate the surface and subsurface waters associated with the lake, and many of the toxins become aerobic when the lake is completely dry.The most important cause of destructive effects of environment and disease in the inhabitants of dried lakes is toxic dust, which causes salt and soil particles to settle on the leaves and stems and the possibility of proper nutrition by animals is eliminated. It is also predicted that with the drying up of the lake, salt-containing precipitation will occur in many neighboring provinces, which will lead to massive migration of people to the cities, which in turn will have irreparable consequences for the region. Salinity agriculture is the exploitation of saline water and soil resources for the production of agricultural and horticultural products, both salinity and non-salinity. Salinization is an economic technology of exploiting saline water and soil resources that cannot be used in conventional agriculture with emphasis on environmental aspects. Saline plants (halophytes) are plants that are able to complete their life cycle in saline soils. These plants 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 to regenerate ecosystems, about 1.11% of the earth's plant flora are salinity-resistant salt marshes. Saline products can even be used as fodder, wood, medicinal and oily plants, etc. Also, with saline agriculture, the pressure on fresh water resources will be less Salicornia is a succulent, succulent, annual plant of the family Chenopodiace and the genus Salicornioideae. The embryo is located in the annular seed or horseshoe and the flowers are complete, the inflorescence is spike and the stem is banded and articulated. About 60 species of salicornia

have been identified so far. One of the most famous species is S. bigelovii (S. bigelovii), which grows in the coastal areas of North and Central America. So far, Mexico, India, Saudi Arabia and the UAE have successfully cultivated salicornia. Out of 15 species of salicornia in the world, there are seven species in Iran. The 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. Due to the diversity that exists in Salicornia, Iran, it is possible to use a suitable species for the climatic conditions of Lake Urmia to exploit the water resources and saline soils of this region. Has been selected and studied as a suitable example for this project.

Methods: According to studies on Salicornia cultivation, Salicornia persica was cultivated in this project. Potting was done with soils of different areas around Lake Urmia, which were randomly selected from every 15 km of the lake and collected in 15 pots. The method of cultivation was that after soil preparation and proper leveling, the pots were irrigated to harden the soil surface. The seeds were then sown to a depth of one centimeter in the soil completely and covered with powdered manure. In order to prevent damage to the delicate seeds of this plant, cultivation was done completely superficially and fertilization was done with more sensitivity and the soil surface was kept moist until the plant was fully established. After about 25-30 days, the results of the study were reviewed and analyzed.

Results: The results of this study showed that cultivation of this plant in the greenhouse is possible by controlling environmental factors and considering the sensitivity of the plant to climatic conditions and photoperiod of the region, soil salinity, the need for special minerals in the early stages of cultivation. . During irrigation of the plant with salt water and drainage, germination is observed for 10 to 20 days. Salicornia is suitable for hot seasons and can not tolerate sub-zero temperatures, so its cultivation in lake lands requires the provision of greenhouse conditions and suitable temperatures in the cold seasons of the year. Excessive irrigation increases the cost of pumping water and creates a large volume of drainage water and leaching of nutrients, so according to the climate of the region and environmental conditions, more studies and research should be done.

Conclusion: The results of the present study are consistent with the results of some studies (Beyrami et al. 1398) and it is possible to exploit the Salicornia plant in the lands of Lake Urmia if the lake is provided with suitable greenhouse conditions. Therefore, in order to enjoy the benefits of planting this plant in the lands of Lake Urmia, more studies should be done to identify and control the interfering factors and adjust the dryland growth conditions of Salicornia plant with greenhouse conditions. In case of planting and growth of

the species, this plant can be used in controlling and stabilizing the soil of saline lands around the lake. Some of the problems in doing this project are: 1- Irrigation in pots is different from irrigation in the field, so in terms of minerals in the samples and the area of soil in which the cultivation was done, more studies should be done. 2- The water used for irrigation in the project was ordinary urban water; But in the fields, the waters around the lake are used, which are different in terms of salinity and salts in them. 3- With each irrigation, the salt in the soil is washed away and the salinity of the soil decreases slightly. Therefore, direct on-farm cultivation is recommended to complete the research.

Keywords: Salicornia plant, Lake Urmia lands, ecosystem

Potential roles of hsa_circ_0043278 in breast cancer and its association with reproductive and clinicopathological factors (Research Paper)

Zahra Firoozi,[1] Elham Mohammadisoleimani,[2] Hosein Mansoori ,[3] Mohammad Mehdi Naghizadeh ,[4] Sedigheh Tahmasebi ,[5] Yaser Mansoori ,[6,*]

1. Department of Medical Genetics, Fasa University of Medical Sciences, Fasa, Iran.
2. Department of Medical Biotechnology, Fasa University of Medical Sciences, Fasa, Iran
3. Department of Medical Genetics, Fasa University of Medical Sciences, Fasa, Iran.
4. Noncommunicable Diseases Research Center, Fasa University of Medical Sciences, Fasa, Iran.
5. Breast Diseases Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.
6. Department of Medical Genetics, Fasa University of Medical Sciences, Fasa, Iran.

Introduction: Breast cancer (BC) causes the highest related death among women worldwide. Years of cancer research provided a great body of evidence that indicates the role of microRNAs (miRNAs) and circular RNAs (circRNAs) in BC. One of the important functions of circRNAs is to sponge miRNAs, which in turn affects the expression of their target mRNAs. In this study, we aimed to assess the expression of hsa_circ_0043278 in breast tumors and normal tissues, and in these contexts, we investigate the potential hsa_circ_0043278/miRNA/mRNA axes.

Methods: We performed total RNA extraction using TRIzol reagent (Invitrogen, USA). After synthesis of cDNA (complementary DNA) according to the manufacturer's protocol (Fermentas, Cat.No: K1622), the expression of hsa_circ_0043278 was analyzed in 50 tumor samples and their adjacent non-cancerous tissues, using quantitative real-time RCR. Also, we assessed the association of hsa_circ_0043278 expression with demographic and clinicopathological information of patients. Then, we used bioinformatic approaches to identify potentially important competing endogenous RNA (ceRNA) networks that are regulated by this circRNA.

Results: hsa_circ_0043278 expression was downregulated in tumor tissues in comparison to adjacent normal tissues. Also, it was found that decreased expression of hsa_circ_0043278 is significantly related to early-onset menarche (age at menarche <14 years in subjects) and larger tumor size (≥ 2.5). The bioinformatics analyses proving that hsa_circ_0043278 has function as a miRNAs sponge regulator.

Conclusion: The current study indicated that hsa_circ_0043278 which show a significant down expression in breast cancer tissues compared with normal adjacent tissues, is related to the age of onset of menstruation and tumor size in studied women. Also, our results suggest that misregulation of various mRNAs could be mediated by hsa_circ_0043278 through sponging the key miRNAs. In addition, hsa_circ_0043278 could be a promising molecular biomarker for BC.

Keywords: hsa_circ_0043278, Breast cancer, Expression, ceRNA, circRNA

Pre-incubation with Kisspeptin improves the adverse effects of the freeze-thawed Human Ejaculated sperms (Research Paper)

Seyede Fateme Hosseini,[1,*]

1.

Introduction: Human sperm cryopreservation can be considered as a common procedure in assisted reproduction technologies (ARTs). In spite of extensive use of cryopreservation in ART programs, it is widely reported that freezing and thawing cause serious detrimental changes in structures (nucleus, membrane and mitochondria) and functions (i.e. motility) of ejaculated spermatozoa. 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.

Methods: Semen samples were collected from 30 healthy subjects, aged 18–35 years, attending cytogenetic clinic in Shiraz, Iran. 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 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 DNA quality 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 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, DNA integrity, Cryopreservation

Pre-operative levels of cell-derived microparticles as a risk factor for post-operative coagulopathy in patients undergoing valve heart surgery (Research Paper)

Mehrnaz Abdolalian,[1] Elham Khalaf Adeli,[2,*] Fatemeh Yari,[3]

1. Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Iranian Blood Transfusion Organization (IBTO), Tehran, Iran
2. Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran
3. Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran

Introduction: Valvular heart disease (VHD) is one of the most common heart problems worldwide. Most VHD patients require heart surgery to repair or replace a defective valve under cardiopulmonary bypass (CPB). Post-operative coagulopathy and bleeding is an important complication of cardiac surgery that increases mortality. Multiple surgical factors such as CPB induce coagulopathy. Cell-derived microparticles (MPs) are membrane vesicles with a size ranges from 0.1 to 1 µm. MPs levels are higher in valve heart disease in comparison to healthy subjects. MPs are procoagulant because they accelerate coagulation cascade and thrombin generation. There are evidences that low levels of MPs are associated with bleeding episodes. Recently, MPs have been used as biomarkers to predict complication of diseases. In this present study, the role of pre-operative MPs as a risk factor for post-operative coagulopathy in patients undergoing heart valve surgery will be investigated.

Methods: This cohort case saries study was performed from January to march 2021 on forty (n=40) adult patients undergoing heart valve surgery with CPB at shaheed rajaie cardiovascular medical and research Center. Plavix was discontinued 5 days prior to surgery and warfarin was discontinued 72 hours before surgery. Patients with anemia, known bleeding disorders, emergency surgery and re-exploration were excluded. Informed written consent was obtained from all subjects. Clinical and laboratory data of patients were collected. Before induction of anesthesia, Venous blood samples were drawn into a plastic vacuum tubes containing 3.2% sodium citrate. MPs were isolated with centrifugation. Total pre-operative concentration of MPs was determined using Bradford method. Flow cytometry analysis was performed to determine MPs count and phenotype using the following monoclonal antibodies: CD41-FITC for platelet-derived microparticles (PMPs) ,and CD14-PE for monocyte-derived microparticles (MMPs).To determine the MPs size and their quantification was used Yellow-green microbeads with 1.0 µm in diameter. Data were analyzed with IBM

SPSS 25.0 statistical software. Post-operative coagulopathy was defined aPTT>48s or INR>1.5. Comparison of concentration and MPs count between coagulopathic and non-coagulopathic patients was performed using Mann-whitney U test. The relationship between pre-operative concentration and MPs count whit post-operative routine coagulation test (INR, aPTT) and ICU(24h) bleeding were assessed using Spearman rank correlation analysis. The role of MPs level as a risk factor for post-operative coagulopathy was performed using univariate and multivariate logistic regression analysis. Statistical significance was considered as P< 0.05.

Results: In post-operative stage, 32.5% of patients were coagulopathic and 67.5% of patients were non-coagulopathic. ICU-bleeding was significantly higher in coagulopathic patients compared to non-coagulopathic patients (P=0.02). The pre-operative MPs concentration was significantly lower in coagulopathic patients compared to non-coagulopathic patients (P=0.006). Comparison of PMPs and MMPs count were not significant between two groups. After correlation analysis, The pre-operative MPs concentration was correlated negatively to post-operative aPTT and INR (Respectively, P= 0.003 ρ=-0.45, P=0.02 ρ=-0.35). The univariate logistic regression analysis for post-operative coagoulopathy indicated that pre-operative MPs concentration led to the elevated risk of coagulopathy (OR 0.988; 95%CI 0.978-0.999; P=0.02). Through further multivariate logistic analysis and considering confounding variables such as CPB time, cross clamp time and operation time, pre-operative MPs concentration was found to be risk factor for occurrence of post-operative coagulopathy (OR 0.989; 95%CI 0.978-0.999; P=0.04).

Conclusion: Considering the role of MPs in hemostasis and accelerating coagulation cascade; in this present study, patients with low MPs concentration in pre-operative stage, had longer routine coagulation tests in post-operative stage. Therefore presurgical MPs concentration was considered as main risk factors for post-operative coagulopathy in patients undergoing heart valve surgery.

Keywords: Cell derived microparticles, Coagulopathy, Cardiac surgery

Preclinical and clinical application of Very Small Embryonic Like (VSEL) Stem Cells in Adult tissues (Review)

Mahsa Rahgoshay,[1,*] Amir Atashi,[2] Mansoureh Ajami,[3] Fatemeh Jamshidi,[4]

1. Department of Hematology and Medical Laboratory Sciences, Faculty of Allied Medicine, Kerman University of Medical Sciences, Kerman, Iran
2. Department of Medical Laboratory Sciences, School of Allied Medical Sciences, Shahroud University of Medical Sciences, Shahroud, Iran
3. Department of Medical Laboratory Sciences, School of Allied Medical Sciences, Shahroud University of Medical Sciences, Shahroud, Iran
4. Department of Hematology and Medical Laboratory Sciences, Faculty of Allied Medicine, Kerman University of Medical Sciences, Kerman, Iran

Introduction: In recent years, stem cell-based therapy became a central focus of interest for their application toward regenerative medicine both from ethical and scientific points of view. Thus, an urgent need is felt for an ethical, reliable, and non-controversial source of stem cells to be established as therapeutics. It has been suggested that a new stem cell population, namely, very small embryonic-like stem cells (VSELs) could potentially provide such a therapeutic alternative to the still controversial application of embryonic stem cells (ESC). VSELs represent a rare homogeneous and highly quiescent population, characterized by their very small size and as being CD34+/CD133+/CXCR4+/Lin−/CD45−. The most important feature is that they demonstrate the ability to differentiate into cells from all three germ layers. Moreover, they express pluripotent) Oct-4, NANOG, and Sox2(as well as an embryonic stem cell (SSEA-4, TRA-1-81) specific markers on their surface. Currently, VSELs have been detected in different adult mouse and human tissues and can be mobilized from the bone marrow into the PB in response to tissue injury including stroke, Acute myocardial infarction (AMI), burn injury, Spinal cord injury, hypoxia or critical leg ischemia. Numerous investigations have already been carried out for murine VSELs, only a few for human VSELs, and all the data have been shown that VSELs can participate in various tissue and organ repair such as the brain, liver, lung, kidney as well as heart and could play an encouraging role in aging.

Methods: Dawn et al. found that at 35 days after MI, VSEL-treated mice had better global left ventricular (LV) systolic performance and reduced myocyte hypertrophy in surviving tissue compared with controls. Moreover, in a study performed by Zuba-Surma et al. VSELs expanded in culture and exposed to a mixture of cardiomyogenic cytokines and growth factors and retain the ability to alleviate LV dysfunction and remodeling after reperfused MI. Anand et al. revealed that VSELs that survive busulphan treatment could potentially regenerate chemoablated mouse testis when healthy niche cells are transplanted via the intertubular route into the testicular interstitium. Other in

vivo experimental models have revealed that transplantation of VSELs could contribute to hepatic and pancreas regeneration as well as hematopoiesis, angiogenesis, and osteogenesis. A recent study demonstrated the involvement of VSELs in the regeneration of mouse bone marrow after 5-fluorouracil treatment.

Results: A phase I non-randomized clinical trial data showed that human VSELs triggered post-ischemic revascularization in immunodeficient mice and acquire an endothelial phenotype both in vitro and in vivo. Moreover, the REGENT-VSEL trial sub-analysis demonstrated that transendocardial injection of autologous BM-derived CD133+ stem cells in patients with chronic refractory angina did not show significant improvement in quality of life in comparison to the control group.

Conclusion: Finally, VSELs isolated from adult tissues appear to be “true” pluripotent stem cells, which could be used, through their progeny, to regenerate damaged organs, and which may solve the problems inherent in the use of controversial embryonic stem cells or induced pluripotent stem cells (iPSCs). These pluripotent stem cells are autologous, embryo-free, patient-specific, and potentially safe for regenerative medicine with no associated sensitive ethical issues as compared to embryonic stem cells.

Keywords: Very small embryonic like stem cells, Stem cells, regenerative medicine

Prediction of potential deleterious nonsynonymous single nucleotide polymorphisms of HIF1A gene: A computational approach (Research Paper)

Zeinab Jamali,[1,*] Mortaza Taheri-Anganeh,[2] Mona Entezam,[3]

1. Department of Medical Genetics, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
2. Cellular and Molecular Research Center, Research Institute on Cellular and Molecular Medicine, Urmia University of Medical Sciences, Urmia, Iran
3. Department of Medical Genetics, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

Introduction: Hypoxia-inducible factor-1α (HIF-1α) is the oxygen sensitive subunit of HIF1 transcription factor. Its variations is associated with several diseases including different type of cancer, cardiovascular diseases, and liver and kidney failure. Despite all the investigations carried out on the single nucleotide polymorphisms (SNPs) of HIF1A gene and diseases, there are many uncharacterized nonsynonymous SNPs of this gene, which might have damaging effect on the protein function. Therefore, it is worthwhile to analyze these potential damaging nsSNPs, using different bioinformatics tools before launching large population studies. The objective of the present study was to predict the possible deleterious nsSNPs of HIF1A gene and their effects on the function and structure of HIF-1alpha protein, using different bioinformatics tools.

Methods: Various prediction servers were used including SIFT, PROVEAN, PolyPhen-2, PANTHER, phD-SNP, SNP-GO, I-Mutant 2.0, Fathmm, SNPeffect 4.0, Mutation taster, CADD and RAMPAGE in a stepwise approach.

Results: After analyzing all 454 missense variants of the HIF1A gene using the abovementioned tools, we reported 11 variants with a significant impact on the function or structure of HIF1 α protein. Furthermore, among these variants only S274 P was predicted as stability enhancing variant with effect on protein function by increasing its stability.

Conclusion: This is a noticeable point that only S274 P is predicted as stability enhancing variant, which might have an effect on protein function by increasing its stability. Although this is a comprehensive computational study, the need for experimental investigations is still warranted.

Keywords: Hypoxiainducible factor1a, Single nucleotide polymorphism, Bioinformatics

Preparation of 17-AAG loaded PLA/PEG Nanofibers for Targeting Genes Hsp90 and hTERT in A549 Lung Cancer Cells (Research Paper)

Sona Talaei,[1,*] Hasan Mellatyar,[2]

1. Department of Basic Sciences, Maragheh University of Medical Sciences, Maragheh, Iran
2. Department of Basic Sciences, Maragheh University of Medical Sciences, Maragheh, Iran

Introduction: The expression of heat shock protein 90 is increased in tumors such as lung cancer cells. 17-allylamino-17-demethoxygeldanamycin (17-AAG) with binding to Hsp90 ATP–binding pocket inhibits the formation of the multi-chaperone complex of Hsp90 that leads to degradation of the Hsp90 client proteins such as hTERT by the ubiquitin-proteasome system. Poor water-solubility of 17-AAG is a fundamental limitation for its clinical application. In the present study, to improve the solubility of 17-AAG, we developed implantable 17-AAG-loaded poly(lactide)-poly(ethylene glycol) (PLA-PEG) nanofibers.

Methods: 17-AAG-loaded PLA-PEG nanofibers were successfully fabricated by electrospinning method and characterized using Field Emission Scanning Electron Microscopy (FE-SEM) and Fourier Transform Infrared (FTIR). The colorimetric cell viability (MTT) assay was performed to evaluate the cytotoxic effects of free 17-AAG and 17-AAG-loaded PLA-PEG nanofibers. Cells were treated with equal concentrations of free 17-AAG and 17-AAG-loaded PLA-PEG nanofibers, and Hsp90 gene expression levels in the two groups were compared by real-time PCR. The effect of 17-AAG and 17-AAG loaded PLA-PEG nanofiber treatment on telomerase activity was monitored by TRAP assay.

Results: MTT assay confirmed that 17-AAG-loaded PLA-PEG nanofibers improved the cytotoxicity of 17-AAG in A549 cells. This finding was associated with a decrease in the expression of the Hsp90 gene and telomerase activity.

Conclusion: The results demonstrated that 17-AAG-loaded PLA-PEG nanofibers are more effective than free 17-AAG in down-regulating Hsp90 expression and inhibiting telomerase activity. Therefore, PLA-PEG nanofiber can be a superior carrier for this kind of hydrophobic agent.

Keywords: Lung Cancer, Hsp90, 17-AAG, PLA-PEG nanofiber, hTERT.

Preparation of 17-DMAG loaded β-cyclodextrin nanoparticles for targeting gene Hsp90 in breast cancer cells (Research Paper)

Hasan Mellatyar,[1,*] Sona Talaei,[2]

1. Department of Basic Sciences, Maragheh University of Medical Sciences, Maragheh, Iran
2. Department of Basic Sciences, Maragheh University of Medical Sciences, Maragheh, Iran

Introduction: Dysregulation of Hsp90 gene expression is found in breast cancer cells. Here we used β-cyclodextrin-17-dimethylaminoethylamino-17-demethoxy geldanamycin (17-DMAG) complexes and free 17-DMAG to inhibit the expression of the Hsp90 gene in the T47D breast cancer cells. The goal was to determine whether nanoencapsulation of 17-DMAG enhances the anti-cancer effects as compared to free 17-DMAG.

Methods: The double emulsion method was used to encapsulate 17-DMAG, and the properties of prepared complexes were characterized by H nuclear magnetic resonance (HNMR) and Fourier Transform Infrared (FTIR). Assessment of cytotoxicity of β-cyclodextrin nanoparticles loaded with 17-DMAG was done by the colorimetric cell viability (MTT) assay. After treatment of T47D cells with a determined amount of free 17-DMAG and 17-DMAG-loaded β-cyclodextrin, mRNA was extracted, and cDNA was synthesized. For assessing the expression of the Hsp90 gene, real-time PCR was performed.

Results: Taking into account 17-DMAG load, IC50 was meaningfully decreased in nanocapsulated 17-DMAG in comparison with free 17-DMAG. This finding was related to a decrease in Hsp90 gene expression.

Conclusion: 17-DMAG- β-cyclodextrin complexes are more effective than free 17-DMAG in down-regulating of Hsp90 expression, at the same time exert more great inhibitory effects. Therefore, β-cyclodextrin can be a superior carrier for this type of hydrophobic agent.

Keywords: Breast Cancer, Hsp90, 17-DMAG, β-cyclodextrin, Nanoparticle.

Preparation of switchable universal chimeric antigen receptors for prostate cancer therapy (Research Paper)

Sheila Seyed Motahari,[1] Shiva Irani,[2] Mohammad Ali Shokrgozar,[3] Shahriyar Abdoli,[4] Zahra Sharifzadeh,[5,*]

1. aDepartment of Immunology, Pasteur Institute of Iran, Tehran, Iran and Department of Molecular Genetics, University of Tehran Science and research Branch, Islamic Azad University, Tehran, Iran
2. Department of Molecular Genetics, University of Tehran Science and research Branch, Islamic Azad University, Tehran, Iran
3. National Cell Bank of Iran, Pasteur Institute of Iran, Tehran, Iran
4. School of Advanced Medical Technologies, Golestan University of Medical Sciences, Gorgan, Iran
5. Department of Immunology, Pasteur Institute of Iran, Tehran, Iran

Introduction: T cells expressing chimeric antigen receptors (CARs) are promising cancer therapeutic agents, with the prospect of becoming the ultimate smart cancer therapeutics. A traditional chimeric antigen receptor has a fixed design, and one type of CAR T cells can only target one antigen epitope. This rigid design limits clinical application and can lead to exceptionally high manufacturing cost. In universal CARs, the antigen recognition domain is split from the signaling domain of a conventional CAR, so the target antigen can be switched or re-directed without re-engineering the CAR T cells. The UniCAR platform has a modular design including a signaling module that binds to a specific epitope on the switching molecule and a switching module with an antigen-binding domain and a switching epitope specifically recognized by the signaling module. In this study the switchable modular CAR T cells will be produced using dimerizing leucine zippers.

Methods: UniCAR constructs were designed using CLC software and synthesized by Biomatik company. The switching module (ZipNb) sequence contains leucine zipper, anti-PSMA nanobody as the targeting moiety, as well as c-myc and his-tag sequences for detection and purification. The signaling module (ZipCAR) contains leucine zipper, CD28 extracellular and costimulatory domains and CD3ς intracellular signaling domain. Both constructs were validated by restriction enzymes and sequencing. The ZipNb gene was subcloned into pET28a vector and transformed into Rosetta DE3 cells. Then the ZipNb expression was induced by IPTG and the expressed protein was analyzed by SDS-PAGE and western blot with mouse anti-c-myc antibody. Protein purification was performed by Ni-NTA column, then the protein dialysis was performed. Two cell lines, LNCaP (PSMA +) and Du145 (PSMA-), were used for nanobody binding evaluation. The ZipCAR gene was subcloned into pLOX vector and transformed into Top10 cells. Extraction of

ZipCAR plasmid was performed by Qiagen Maxi purification kit. By reverse transfection procedure, ZipCAR, psPAX and pMDG2 plasmids were tranfected to LentiX 293 T cell line to produce lentiviral particles. These transfected cells were incubated for ~3 days post-transfection. Then, the culture medium (virus-containing supernatants) was harvested and used to transduce HEK293 and target T cells. Finally, transduced Jurkat T cells were evaluated for the universal CAR T cell expression.

Results: In the present study, we prepared uiversal CAR T cells to targeted prostate cancer cells. The ZipNb containing anti-PSMA nanobody was expressed in different conditions. Our findings showed that the highest ZipNb expression was observed in Rosetta DE3 after 16 hours post-induction by 1mM IPTG, and in 37 ˚C. SDS-PAGE and western blot analysis proved the expression of the desired targeting module with the molecular weight of about 27 KDa. Flow cytometry results confirmed the ZipNb binding to PSMA antigen on target prostate cancer cells. The ZipCAR containing lentivirus were concentrated, titrated and used to transduce HEK293 and and Jurkat cell lines. Flow cytometry results showed the ZipCAR expression on the surface of transduced cell lines.

Conclusion: The modular UniCAR designs make it possible to re-engineer a variety of switchable and programmable UniCARs .The switch molecule makes a synapse between the CAR T cells and the target tumor cells. For CAR T immunotherapy to realize its potential target in solid tumors, addressing tumor heterogeneity and enhancing its safety profile are the main problems for its use in the clinic. An adaptable system such as modular CAR T cells conceivably could address these issues by tailoring CARs to a patient's specific cancer and adapting treatment using a toolkit of adaptor targeting elements. The UniCAR T cells developed in this study could be promising tools to target different cancer antigens. However, functional assays are needed to prove the anti-tumor effect of these UniCAR T cells on prostate tumor cells.

Keywords: Cancer immunotherapy, Universal CAR T, PSMA, Prostate cancer, Nanobody.

Prevalence of depression and its related factors in infertile women: A review article (Review)

Mohammad mahdi mohammadi,[1,*] zeinab sadat moosavifard,[2]

1. BSc in Nursing, Department of Nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.
2. Department of Nursing, faculty of nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.

Introduction: Infertility means not being able to conceive for a year without having to use contraception. Infertility can affect many aspects of infertile women's lives and cause sexual dysfunction, depression, hopelessness, and feelings of guilt and worthlessness. The aim of this study was to investigate the prevalence of depression and the factors affecting it in studies.

Methods: In this review article, relevant and appropriate Persian and English articles were collected from the Persian and English electronic databases of students, University Jihad, Google Scholar, Pubmed Science Direct, using the keywords infertility, infertility, depression and mental disorders from 2001 to 2018. Among the related articles, 29 articles were in line with the objectives of the study that were reviewed.

Results: The prevalence of depression was reported in studies between 79.5-79%. Findings of studies showed that in total, factors related to depression in infertile women include 1. Demographic variables such as (age of the couple, education of the couple, working conditions of the women, duration of marriage, place of residence of the couple, treatment costs, financial burden Physicians) 2- Factors related to depression in disbelief Primary type of fertility, duration of infertility, cause of infertility, history of infertility treatment, history of failure in infertility treatment such as (primary type of infertility, duration of infertility, history of infertility treatment, general history of success in infertility treatment, history of abortion, number of treatments 3- Family factors such as (irrational parents, being pressured by family and relatives, poor support of the spouse, the level of marital satisfaction) 4. Psychological factors such as (low self-esteem, stress, social worries, sexual anxiety, perceived social support).

Conclusion: According to studies in this field, mental health interventions by health care personnel and also the emphasis on psychological support of families from the time of infertility diagnosis and during the treatment process can help reduce the rate of depression in them.

Keywords: Depression, infertility, review study

Prevalence of virulence factors and antibiotic resistance in lactic acid bacteria isolated from traditional dairy products (Research Paper)

Armin Moghadam,[1] Mohammad Javad Rezaei,[2] Ehsan Sohrabi ,[3] Seyed Saeed Mirdamadi,[4] Mohammad Mohammadi,[5] Ali Naghoni,[6,*]

1. Research and Development Unit, Fara Daru Fanavar Mehr Pharmaceutical Co., Tehran, Iran
2. Research and Development Unit, Fara Daru Fanavar Mehr Pharmaceutical Co., Tehran, Iran
3. Research and Development Unit, Fara Daru Fanavar Mehr Pharmaceutical Co., Tehran, Iran
4. Iranian Research Organization for Science and Technology (IROST), Tehran, Iran
5. Fara Daru Fanavar Mehr Pharmaceutical Co., Tehran, Iran
6. Research and Development Unit, Fara Daru Fanavar Mehr Pharmaceutical Co., Tehran, Iran

Introduction: Lactic acid-producing bacteria are the most commonly used probiotics in foods and dietary supplements. It is well known that probiotics have a number of beneficial health effects in humans and animals. Probiotics are distinguished by astonishing criteria: improving the balance of the microbiota inside the intestine, inhibiting pathogenic microorganisms in the gastrointestinal tract, adjusting the intestinal environment, ability to reduce pathogen adhesion activity, capabilities of regulating intestinal mucosal immunity, and maintaining intestinal barrier function. Since these bacteria are typically viable when consumed, considerable characterization is required to ensure the absence of undesirable properties.

Methods: In this study, 244 strains from different sources of traditional dairy products such as, yogurt, yogurt drink, milk, and butter were collected from different regions of Iran. 18 out of 240 LAB isolates were selected due to their primary probiotic properties (resistance to low pH, bile tolerance, and tolerance to pepsin and trypsin) and identified by phenotypic and 16S rRNA gene sequence analysis. The 20 isolated species were assessed for the incidence of virulence genes (gelE, efaAfm, efaAfs, ace, espfs, cylM, cylA and cylB), sensitivity to different antibiotics. The incidence of virulence genes was determined by polymerase chain reaction and antibiotic susceptibility was assessed by disk diffusion method.

Results: The dominant bacterial genera isolated were Lactobacillus, Lacticaseibacillus, and Bifidobacterium. Also, the results of this study showed no virulence genes for all 20 isolated species. In addition, minority of strains showed only low level of resistance to rifampicin and chloramphenicol and were sensitive to all other antibiotics tested for.

Conclusion: The results of this study showed that our isolates can be good candidates for using as a probiotic. However, for further assessment, it is recommended that whole-genome sequencing of each strain be performed.

Keywords: Virulence factor, antibiotic resistance, lactic acid bacteria, dairy products, 16S rRNA

Prevalence, distribution of capsule serotypes, and resistance antibiotics of Streptococcus agalactiae among Iranian women from 2006 to 2020: A Review Analysis (Review)

Zahra Zareh,[1,*] Maryam Keshtvarz,[2] Mohammad Ali Haghighi,[3] Saeed Tajbakhsh,[4]

1. Bushehr University Of Medical Sciences, Bushehr, Iran
2. Bushehr University Of Medical Sciences, Bushehr, Iran
3. Bushehr University Of Medical Sciences, Bushehr, Iran
4. Bushehr University Of Medical Sciences, Bushehr, Iran

Introduction: Group B Streptococcus (GBS) is an opportunistic pathogen, especially in pregnant women, and is one of the leading causes of infant mortality worldwide. So, finding the prevalence of this pathogen along with its antibiotic resistance are vital in vaccine development. Also since the polysaccharide capsule plays an important role in the pathogenicity of GBS, the identification of various serotypes of the capsule can be important for epidemiological studies and vaccine production. Our aim was to do a review analysis of the prevalence, antimicrobial resistance patterns, and capsule serotype distributions of GBS in Iranin pregnant women in 28-40 weeks of pregnancy.

Methods: We searched the PubMed/Medline, Embase, and Iranian national databases for research published during 2006-2020, and identified 42 studies.

Results: Overall prevalence of GBS in pregnant women was 13.2%. The highest prevalence of resistance was reported for second-line drugs such as tetracycline followed by clindamycin and erythromycin. Moreover, serotype III was the most common capsule.

Conclusion: Due to the significant percentage of the prevalence of GBS in Iranian pregnant women, and to prevent infection of newborns, screening of this bacterium during pregnancy is recommended. Ampicillin can still be an effective drug in the treatment of GBS; however, in women who are allergic to ampicillin and penicillin, antibiogram testing should be performed before prescribing with second-line drugs. Overall, maternal vaccination, especially with serotype III is a better option.

Keywords: Group B Streptococcus, antibiotic resistance, Capsule.

Prevention, Diagnosis, and Treatment of Glioblastoma (Review)

Mohammad Javad Makatian ,[1,*] Ali Asghar Abbasi Rozgole,[2] Shahabeddin Madani,[3] Aidin Shojaei ,[4]

1. Shahid Motahari School
2. Shahid Motahari School
3. Nikparvar school
4. Allameh Hali 5 school

Introduction: The most general primary brain tumor in adults is gliomas. Gliomas measure a diapason from low to high grade and are graded pathologically on a scale of one to four according to the World Health Organization classification. Grade IV glioma is acknowledged as Glioblastoma. Glioblastoma (GBM) is a malignant brain tumor that grows quickly by building blood vessels around it and easily damages brain texture. Glioblastoma is not very common but is 20% more probably to develop brain cancer. And 2.5 percent of deaths are due to cancer. Glioblastoma is ordinary in men and is usually seen in the average age of 64. Glioblastoma starts from astrocyte cells and in adults in the cerebrum (forebrain). Glioblastoma seldom spreads outside the brain, and factors that because glioblastoma include exposure to certain substances, chromosome changes, and family-specific inherited disease. Because glioblastomas grow quickly, pressure on the brain usually causes the first symptoms. Depending on where the tumor is, it can cause persistent headaches, double or blurred vision, vomiting, loss of appetite, changes in mood and personality, change inability to think and learn, new onset of seizures, and speech difficulty of gradual onset. A neurologist will give you a complete exam. The complete exam includes sophisticated imaging techniques (which can accurately pinpoint the location of brain tumors.), computed tomography (CT or CAT scan), and magnetic resonance imaging. Magnetic resonance spectroscopy is used to examine the tumor's chemical.) The Common treatment for recently diagnosed glioblastoma is surgery to remove as much of the tumor as possible, followed by chemotherapy (an anti-cancer drug called temozolomide; TMZ) and radiotherapy. TMZ is often given concomitantly with radiotherapy (concomitant chemotherapy), and also lasts for about 6 months after radiotherapy (adjuvant chemotherapy). simultaneously, these treatments are also known as chemoradiotherapy. However, not all people, especially the elderly, are good enough to get a CRT because it can have serious side effects.

Methods: The present study was considered the first joint research work by this group. So, to start the research, we studied and searched online resources. Research has been done on various methods that prevent, diagnose and treat glioblastoma. To collect information, we referred to various

articles in the period 2017-2021. We reviewed the collected material in several online sessions. Eleven articles have been used to compile this collection, which according to the previous information and with the knowledge of four articles have been rejected and the necessary conclusions have been made from eight articles in total. After discussion and exchange of views, the final text was prepared.

Results: Glioblastomas are malignant tumors with grade 4. A large portion of the cells in these tumors are constantly proliferating and dividing. These cancer cells are nourished by abundant and abnormal blood vessels. Glioblastoma can present as a grade 4 tumor from the beginning and there is no sign of lower-level tumors. These tumors are the most common type of glioblastoma, affecting most older patients, and are more aggressive than other tumors. Glioblastomas can be difficult to treat because of the resistance of some cells to treatment. For this reason, a glioblastoma treatment plan may include several treatment strategies.

Conclusion: The glioblastoma brain tumor is a type of brain cancer. The most common type of malignant brain tumor in adults is glioblastoma. This tumor is highly invasive, meaning it has a high growth rate and spreads rapidly. Brain tumors that originate from astrocyte cells occur mostly in adults in the frontal lobe of the brain. Glioblastoma brain tumor grows by creating blood vessels around it and easily destroys other healthy brain tissue. Brain tumors are not very common, but if they occur in less than 20% of cases, it may be glioblastoma, which is likely to cause a tumor. Glioblastoma is more common in men than women and increases with age. Because glioblastoma grows swiftly, the first complication is pressure on the brain. Depending on what area of the brain the tumor is in, any of the complications mentioned in the article may occur. The goal of tumor treatment is to control growth and metastasis and help eliminate the complications of the tumor. There are several treatment strategies for brain tumors, the most important of which is surgery.

Keywords: glioblastoma, Glioma, Brain Tumor

Prevention of leukemia Treatment (Review)

fatemeh kotalan,[1,*]

1. Islamic Azad University, Dezful Branch

Introduction:

A disease that begins with the abnormal proliferation of cells in the body is ge nerally called cancer, but if this disorder occurs in the process of producing bl ood cells, it is called leukemia. In such cases, the cells can no longer do their normal work and may number. Too much and out of control. Therefore, blood can not do its job properly. Leukemia usually starts in the bone marrow and ca uses a large number of abnormal white blood cells to form. Cancer, which is t he second leading cause of death in the world, is divided into three types: leuk emia
lymphoma and myeloma. It may spread over a short period of time in the body , called an acute condition, or in the long term with a slow growth that is called a chronic condition. The cause of leukemia is unknown, but factors such as a family history of leukemia, smoking, disorders Genetics such as Down syndro me Blood disorders, such as myelodysplastic syndrome, history of cancer trea tment with chemotherapy, exposure to high radiation increases the risk of leuk emia, including the symptoms of this disease in both women and men can sw eat more than Limit, especially at night, fatigue and weakness that does not g o away with rest, unwanted weight loss, bone pain and painless swollen lymp h nodes (especially in the neck and armpits), red spots on the skin, called pet echiae, fever or Shivering and ... but to diagnose the disease Tests such as a complete blood count can determine the number of red blood cells, white bloo d cells, and platelets in the blood. Or biopsies of bone marrow or lymph nodes that can show the type and rate of cancer growth, and biopsies of other organ s such as the liver and spleen can be used to detect the spread of cancer. To diagnose the disease, several other tests can be used, such as DNA flow cyt ometry Which examines cancer cells and determines their growth rate. Or a lu mbar puncture is done by inserting a thin needle between the lumbar vertebra e. This allows the doctor to collect spinal fluid and determine if the cancer has reached the central nervous system. Use Treatment for this disease varies de pending on the type of cancer and the stage at which it is diagnosed. One met hod of treatment is energy radiotherapy. It is used to damage leukemia cells a nd inhibit their growth, or to use biological therapy that helps the immune Sys tem to detect and attack cancer cells. Other treatments include stem cell transplantation Of course ,the yonuger the person and the lack of a history of blood disorders and chromosomal mutations,the better the treatment process and the greater the chances of rescovery

Methods:

The present study is a systematic review study that was performed from searc

hing databases and Google search engine choleraelementElsevierSid with th e keywords cancer, treatment, leukemia, prevention without time limit and out of all the articles found,
8 articles were in accordance with the purpose of the diagnosis study. And wa s used

Results:
Based on the above, it can be concluded that information on the main cause o f leukemia is not available, so we can not do an exact solution to prevent this disease, but people who have even one of the possible causes of this disease are factors. Like smoking, exposure to radiation, having a family history of thi s disease and other factors mentioned above, it is better to have a complete c heck-
up every six months or every year, because the sooner this disease is diagno sed, the more it can progress and the treatment process. It will be more effecti ve.

Conclusion: In general, cancer is one of the diseases that have a difficult and long treatment process, the sooner it is diagnosed, the better the treatment process and the percentage of chances of complete recovery

Keywords: Cancer, leukemia, treatment, prevention

Production of anti-dust mask from silver nanofluid (Review)

Arshin Mirabi,[1,*]

1. Experimental tenth grade student of Andisheh State Model School, Semnan, Iran

Introduction: The use of processes based on nanomaterials and nanotechnology is growing rapidly in all fields of science and technology, and due to the problems of the dust crisis in the south and southwest of the country and air pollution in metropolitan cities and industrial cities, the production of anti-spandband Bacterial has many uses to reduce contamination and stop the growth of various contaminants (germs, viruses and bacteria). The present paper has been carried out with the aim of producing antibacterial mask from silver nanofluid by library and experimental method in laboratory environment. The results of this article can help reduce the dust crisis and respiratory problems of patients, especially in metropolitan areas.

Methods: Checking antibacterial tests , halo and using standard and valid cards such as: books, ISI articles, etc.

Results: Observations of the diameter of the halos show that spunbond filters are resistant to standard bacteria, especially at 4000 ppm, and reduce bacterial growth by a large percentage and have the greatest antibiotic effect. The filter with a concentration of 2000 ppm and then a filter with a concentration of 1000 ppm had an antibiotic effect. Also, by examining the quantitative results of antibacterial test by Behprovar Salamat Laboratory and approved by the Food and Drug Administration regarding bacterial growth of a sample with an optimal concentration of 4000 ppm in the vicinity of five different types of standard bacteria shows that the number of bacteria in culture medium adjacent to the sample The coating remained constant and bacterial growth and proliferation did not happen.

Conclusion: Air pollution is one of the most important problems of metropolises and industrial cities that has caused numerous respiratory problems in the people and the presence of fine dust in the south and southwest of Iran has caused respiratory diseases and many problems for the people. The production of antibacterial spunbond masks from silver nanofluids produced in this study, helps a lot to the diseases mentioned, and can be a suitable and cost-effective alternative for these patients. Also, the simple and low-cost coating method with immersion method in this research to produce antibacterial spunbond from silver nanofluid is a suitable alternative to previous time-consuming and cost-effective methods.

Keywords: Keywords: Mask, Antibacterial, Pollutants, Silver nanofluid.

Protective effect of betanin against 6-hydroxy dopamine induced cell toxicity in PC12 Cells (Research Paper)

Elham Hadipour,[1,*] Zahra Tayarani-Najaran,[2] Masoud Fereidoni,[3]

1. University of Guilan
2. Mashhad University of Medical Sciences
3. Ferdowsi University of Mashhad

Introduction: Parkinson's disease is a neurodegenerative disorder which accompanied with cognitive decline, chorei form moves and behavioral difficulties. This study aimed to investigate the protective effect of betanin on toxicity and oxidative damage induced by 6-hydroxy dopamine (6-OHDA) in PC12 cells as an appropriate model similar to Parkinson's cell damages.

Methods: PC12 cells were pretreated with betanin (1-200 µM) for 24h and then exposed to 6-OHDA (100 µM) for 24h. At the end, the cell survival, intracellular reactive oxygen species (ROS) production assessed by analysis of cell viability, ROS generation. Also the anti-apoptotic effects of betanin in PC12 cells were studied using flow cytometry after PI staining.

Results: betanin (1-200 µM) could decrease 6-OHDA (100 µM) toxicity and showed significant difference compared to the 6-OHDA group ($P<0.05$, $P<0.01$ and $P<0.001$). After exposure of cells to 6-OHDA (100 µM) for 24 h, betanin (1-200 µM) significantly decreased ROS ($P<0.001$). Cell apoptosis was significantly increased to 75.9% after treatment with 6-OHDA (100 µM) compared to control (1.9%). After pretreatment with betanin (20 and 50 µM); however, apoptosis was significantly reduced to (15.3% and 31.3%).

Conclusion: Our study revealed that betanin may exhibit protective effect on the apoptosis induced by 6-OHDA in PC12 cells, possibly by reducing oxidative stress. Thus, betanin may be considered as a valuable candidate drug for the treatment of Parkinson's disease

Keywords: Parkinson's disease; 6-OHDA; betanin

Protective Effect of Nano Emulsions Containing Rosemary on Hippocampal CA1 Pyramidal Neurons in a Rat model of Cerebral Ischemia-Reperfusion (Research Paper)

Zahra Abbasy,[1,*]

1. Faculty of Medicine, Kashan University of Medical Sciences, Kashan, Iran

Introduction: Stroke is an important cause of mortality and morbidity worldwide but effective therapeutic strategy for the prevention of brain injury in patients with cerebral ischemia is lacking. Rosemary is a plant that have strong antioxidant and anti-inflammatory effects that may be helpful.

Methods: This study had two main parts: In vivo and in vitro. In in vivo part, we divided wistar rats into 8 groups (control, ischemia/reperfusion, 3 dose of aqueous- alcoholic extracts of rosemary and 3 dose of aqueous extracts of rosemary), after 21 days of rosemary administration the ischemia and reperfusion was done, finally apoptosis gene and neurons death were assayed in hippocampus and in in vitro part we cultured hippocampus neurons (in 7 groups: control, 3 dose of aqueous extracts of rosemary and 3 dose of aqueous-alcoholic extracts of rosemary) and then cell viability was assayed.

Results: We demonstrated that 200 mg/kg aqueous extracts of rosemary decrease the apoptosis gene expression and increase the anti-apoptosis gene expression in compare to ischemia ($p<0.05$) and decrease the neuron death in Hippocampal CA1 pyramidal neurons ($p<0.05$).

Conclusion: Present study demonstrated that cerebral ischemic tolerance induced by rosemary extracts pretreatment, the aqueous-alcoholic extracts of rosemary in 200 mg/kg dose was more effective to protect of hippocampus.

Keywords: Protective, Nano Emulsions, Rosemary, Hippocampal, Ischemia /Reperfusion

Protective Effects of Antioxidants on Testicular tissue against Aluminum exposure (Review)

Seyed Sobhan Bahreiny,[1,*] Mohammad Reza Dabbagh,[2]

1. Department of Biology, University of Qom, Qom, IRAN
2. Department of Biology, University of Qom, Qom, IRAN

Introduction: Numerous factors can affect male fertility, Reproductive toxicity is a major challenge associated with aluminum (Al) exposure which in the last 3 years, has published many articles in databases. High utilization of Al-containing products will increase the concentration of this metallic element in the consumers' organs and damage their various tissues (including the testicular tissues of humans and animals). Therefore, the present review study was conducted to determine the role of the protective effect of some Antioxidants substances on male fertility.

Methods: In this study, PUB MED / SCOPUS databases from 2017 to 2020 were searched for related articles. In this systematic review, we intend to analyze and evaluate greater than ten powerful elements in growing the fertility of men who've been exposed to Al, such as Curcumin, Tyrosol , esculetin , Melatonin , L-arginine,vitamin E, vitamin E-selenium combination, Propolis , Piper Guineans, pomegranate liquid. Aluminum (Al), the third most common element in the Earth's crust, has significant toxic potential for humans. Although Al toxicity was initially recognized as a neurological, in recent years the destructive effects of Al on reproductive tissues and their function have received more attention. Moreover, high levels of Al in spermatozoa and seminal plasma of humans have been reported to reduce sperm viability and motility Al may cause male reproductive toxicity through various mechanisms such as inducing oxidative stress, interfering with spermatogenesis and steroidogenesis, impairing cell signaling, disrupting the blood-testis barrier, and affecting the endocrine system Antioxidants (AO) are compounds that prevent oxidation. In the tissue, they interrupt oxidative chain reactions.In recent years, increasing attention has been paid to the use of nutritional antioxidants (such as plant products) in diseases related to oxidative stress. The protective effects of natural products have been attributed to their role in eliminating free radicals and antioxidant defense regulators. As a free radical scavenger, these substances can greatly inhibit the production of reactive oxygen species (ROS) both in vitro and in vivo. It also has anti-cancer, anti-inflammatory and anti-bacterial properties But their most important effect is to reduce testicular tissue apoptosis by reducing oxidative stress as well as increasing sperm motility and quality.

Results: considerable reductions in body and testis weight; plasma testosterone and luteinizing hormone levels; sperm count, motility,

morphology, and viability; germinal epithelium thickness; seminiferous tubules diameter; as well as, superoxide dismutase activity were observed in rats exposured with Al. antioxidants treatment significantly improved morphological normality and sperm count, motility, and viability in rats receiving Al chloride. . but ,No significant differences in gonadotrophin (FSH) levels and nuclear diameter of spermatogonia were detected among all groups.

Conclusion: in rats receiving antioxidants(AO) considerably reversed the adverse effects of Al on testicle gland and spermatozoon quality, In other words, AO may counteract the negative effects of Al within the mentioned-reproductive parameters.

Keywords: Aluminum, Aluminum Toxicity, Male Reproductive System, Oxidative Stress, Sperm Motility

Provide immunity protection against Acinetobacter baumannii by exposed loops of BauA and Omp34 in a murine model (Research Paper)

Zahra Akbari,[1] Iraj Rasooli,[2,*] Anthony B. Schryvers,[3]

1. 1 Department of Biology, Shahed University, Tehran-Iran
2. Molecular Microbiology Research Center and Department of Biology, Shahed University, Tehran-Iran
3. Department of Microbiology, Immunology and Infectious Diseases, Cumming School of Medicine, University of Calgary, Canada

Introduction: Acinetobacter baumannii causes a wide range of infections due to its persistence and ability to survive and adapt in the hospital environment. Due to the resistance of this bacterium to various drugs and its prevalence, basic strategies are needed for the prevention and treatment of related diseases. Omp34 is one of several pathogens of Acinetobacter baumannii that its important role in the pathogenesis and survival of this bacterium has been proven. According to studies and understanding the important role of protein BauA (Baumannii Acinetobactin Utilization), which is produced under iron deficiency conditions and is required for the transfer of acinetobactin (iron-containing siderophore) to bacterial cells, makes it necessary to use BauA and Omp34 to make vaccines.

Methods: By examining the BauA and Omp34 immunogenic regions, the loops with the highest bioinformatics immunogenicity scores were selected. Using a new hybrid antigen method in which superficial epitopes of the TbpA receptor protein from Neisseria meningitidis are displayed on the C-lobe of a TbpB surface lipoprotein called Loopless C Lobe or LCL. After designing specific primers from the desired genes and regions and gene amplification, for replication, the amplified fragment was treated with a vector in the desired enzymatic digestion reaction. Then, using ligase enzyme, the digested fragment was SOE-PCRed into the LCL at the designated position, and the resulting fragment was inserted into the expression vector. The recombinant proteins were expressed and purified using a Ni-NTA column. After the immunization of the laboratory animal, the production of antibodies against the recombinant proteins was assessed by indirect ELISA. The animal challenge was performed in active and passive immune groups and the survival of the challenged control and immunized mice were evaluated. The microbial load on lung, spleen, and liver organs was counted.

Results: The hybrid antigens produced in the cytoplasm of E. coli were expressed as soluble antigens. The antigens were used to immunize mice, followed by challenge trials with A. baumannii clinical isolate (ABI022). Mice immunized with the combination of BauA7 loop (BauAL7P3) and Omp34 loop 3 (Omp34 L3P1) provided a 71.43% survival rate against A. baumannii

infection. Each single protein group showed 42.86% protectivity on the basis of survival rate. A significant reduction in microbial load was evident in the lungs, livers, and spleens of the immunized groups.

Conclusion: The results show that immunization with the immunogenic loops causes a strong protective reaction in the mouse model. The findings support the use of multiple antibodies to induce wider reactive antibody responses against heterogeneous strains of Acinetobacter baumannii.

Keywords: Immunogenicity., Vaccine., BauA., Omp34., Acinetobacter baumanni

Provide immunity protection of avian immunoglobulin (IgY) against the recombinant VacJ protein of Acinetobacter baumannii in a model of mouse pneumonia (Research Paper)

atefe sharifi,[1,*]

1.

Introduction: Acinetobacter baumannii is one of the pathogens in clinical settings that can cause a variety of infections. The lack of effective antibiotics is convincing researchers to consider new treatment options. Many bacterial lipoproteins are involved in escape from the host immune system, and antibiotic resistance. Therefore, lipoproteins are good options for inducing immunity against many infectious diseases. The VacJ gene is highly conserved and produces an outer membrane lipoprotein that is associated with virulence in many pathogens. as a result, VacJ as a membrane lipoprotein is a suitable target for vaccine design and production.After immunization of laying hens by recombinant proteins (VacJ).

Methods: IgY was purified from the egg yolks.Then, ELISA immunoassays were performed and the protective effect of antibodies was evaluated in a mouse model of A. baumannii pneumonia

Results: Injection of VacJ antigen stimulated the immune system of chickens well. After purification and collection of chicken antibodies to evaluate the protective effect of this antibody, nasal form was given to mice with weakened immune system and then mice were infected with Acinetobacter baumannii. Infected, survival and cultured lung and spleen were assessed. There was a significant difference between the survival of immunocompromised mice with other groups.

Conclusion: Partial protection of avian antibodies against VacJ resulted in 100% survival of the group receiving anti-VacJ antibodies. Also, in organ culture, a significant reduction in bacterial load was observed in the group receiving safe antibodies. Our results showed that VacJ antigen is effective in prevention and is a good candidate for vaccine design.

Keywords: VacJ, Acinetobacter baumannii , pneumonia , immunization egg yolk (IgY

Quality of Breast Cancer Pathology Reports in three Different Hospitals in Urmia, Iran (Research Paper)

Fariba Abbasi,[1,*] Hushyar Azari,[2]

1. Solid Tumor Research Center, Cellular and Molecular Medicine Institute, Urmia University of Medical Sciences, Urmia, Iran
2. Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran

Introduction: This study was conducted to investigate the quality of standard criteria utilized in reporting breast cancer pathology and to compare the variability between public and private hospitals.

Methods: In this retrospective study, three hundred and fifty pathology reports of mastectomy samples with diagnosis of primary breast cancer were retrieved from archives of pathology departments of three hospitals in Urmia, Iran; one public teaching (121), one public nonteaching (99) and one private hospital (130). The reports were assessed according to the College of American Pathologists(CAM) criteria for macroscopic and microscopic characteristics including tumor laterality, color, size, type and grade, consistency, size of the sample, description of prior biopsy site, condition of the specimen (fresh, or in fixative), number of excised and involved lymph nodes, previous frozen section (FS), surgical margins, lymphovascular invasion and insitu carcinoma.

Results: None of the reports had all the suggested items. Specimen condition was the only item recorded in all of the reports. The teaching hospital reports had significantly higher number of reported items than 2 others ($P<0.001$). Four items including tumor laterality, sample size, number of excised lymph nodes and number of involved lymph nodes were indicated in more than 90% of reports. On the other hand, non-tumoral breast changes and previous F.S were reported in less than 10% of reports. Key items including tumor size, type and grade, surgical margin, vascular invasion, carcinoma insitu were also indicated more frequently in the teaching hospital ($P<0.001$).

Conclusion: We showed evident variations in reporting of breast cancer pathology in different hospitals. It seems that the teaching program in the public-teaching hospital can be a reason for the better results in this hospital. So we suggest using standard worldwide protocols for cancer reporting and also creating an effective audit system to evaluate complete utilization of the protocols.

Keywords: Breast pathology, Cancer, Reporting, tumor

Rapid methods of diagnosis Neisseria meningitidis (Review)

Maryam Rad,[1] Gholamhossein Ebrahimipour,[2] Mojgan Bandehpour,[3,*] Omid Akhavan,[4] Fatemeh Yarian,[5]

1. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
2. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
3. Cellular and Molecular Biology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran-Department of Medical Biotechnology, School of Advanced Technologies in Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
4. Department of Physics, Sharif University of Technology, Tehran, Iran
5. Cellular and Molecular Biology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran-Department of Medical Biotechnology, School of Advanced Technologies in Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Introduction: Neisseria meningitidis is one of the main causes of the spread of meningitis in the world, which is a gram-negative bacterium that the only host of this bacterium is humans[1]. Of the 13 serogroups (A, B, C, D, E, H, I, K, L, W, X, Y, and Z) of this bacterium that are classified based on polysaccharide capsules, five serogroups (A, B, C, Y, W-135) are the cause of most diseases in humans, with serogroups A and C being the most common cause of meningococcal meningitis. But severe epidemics caused by B, Y and W-135 groups have also been seen. Despite the declining prevalence of meningitis due to vaccination, bacterial meningitis is still a public health problem, with about 200,000 people dying from bacterial meningitis worldwide each year, with up to 60% of deaths reported in sub-Saharan Africa and developing countries. If treated, this rate is reduced to 10%, but most serious complications such as amputation, nerve defects and other serious disabilities have been observed in the survivors. The main methods of diagnosis of Neisseria meningitidis in most parts of the world are PCR, ELISA and culture, which is a authentic standard PCR [2]. Standard reference methods have the following problem: • Requires an experienced technician and equipped laboratory Among the limitations of cultivation, we can mention such things as: • The possibility of sample contamination during storage or improper transfer • Effects of initial antibiotic treatment [3] People of all ages are at risk for life-threatening meningococcal meningitidis. Because the disease can cause permanent damage to the central nervous system or cause death within a few hours, it is important to know the disease quickly [4]. Rapid diagnostic tests: According to the International Organization for Standardization (ISO), the point-of-care test (POCT) is defined as a test that allows a change in a person's care to be made by allowing the patient to be

examined on or near the patient's site. One type of care point test is a rapid diagnostic test (RDT). Rapid diagnostic tests qualitatively or semi-quantitatively identify antigen or antibody in a patient sample [5]. Rapid diagnostic tests can detect Neisseria meningitidis in a cerebrospinal fluid (CSF) specimen without the need for initial preparation (centrifugation or heating). Detection of antigen in CSF sample by antibody coated on the surface of gold nanoparticles and nitrocellulose membrane, ie immunochromatography, is the basis of the performance of these tests. These tests have advantages such as cost-effectiveness, mass production, and stability in hot weather for weeks. The basis of the work is that the test is immersed in the tube containing the sample and after a period of time about 10 to 15 minutes, the result is checked. The color change indicates that the test is positive [6]. Figure 1 shows a schematic of a rapid diagnostic test based on immunochromatography [7].

Methods: After searching in databases such as Google Scholar, Pub Med and Science Direct, related articles were selected and used.

Results: Because effective treatment of meningitis requires identifying the pattern of antibiotic susceptibility of the bacterium, as well as common diagnostic methods such as culture, it is time consuming and the bacterium may not grow [10], so rapid diagnostic tests are important. These tests can also be used as a supplement. For example, in addition to clinical picture and CSF examination, you can use rapid diagnostic tests, the positive results of which indicate a possible infection with the bacterium Neisseria meningitides [6].

Conclusion: Despite the development of rapid diagnostic tests in recent years, these tests still need to be optimized. Due to the problems mentioned in Table 1 and on the other hand the importance of rapid diagnosis of meningitis, we need tests that can be sufficiently effective and on the other hand the problems mentioned in their design have been minimized.

Keywords: Neisseria meningitidis, Rapid test, meningitis

Recent advances in the design and fabrication of rapid paper-based carbon dots for antibiotics detection (Review)

Sana sadroleslami,[1,*] zeinab bagheri,[2] mohammad yaghoubi avini,[3]

1.
2.
3.

Introduction: In addition to treating infectious diseases, antibiotics made many modern medical procedures possible, including cancer treatment, organ transplants, and open-heart surgery. However, the misuse of these valuable compounds has led to a rapid increase in antimicrobial resistance, and some infections are currently not effectively treatable [1]. According to the WHO, antimicrobial resistance is considered one of the most serious global threats, increasing many drug-resistant diseases and infections in the near future. Antibiotics are mutant and resistant bacteria. They do not kill the drug and only kill the infected bacteria. These drugs are not completely metabolized in the human or animal body, so they are excreted into the environment and enter the food cycle through animals and the environment. Besides, antibiotics can indirectly reach humans through meat and dairy products, as they are widely used in veterinary medicine [2]. Therefore, developing more accurate, faster, and cheaper methods for detecting antibiotic residues in the environment and food is of great importance [3]. In recent years, rapid tests for detections have got a special place in the world. For example, nowadays, paper-based pregnancy tests are very popular and valuable. Paper-based biosensors have made it possible to create flexible, simple, and portable diagnostic devices at low cost [4]. The main advantages of paper are absorption properties, Capillary action, large surface-to-volume ratio, and functionalization with various functional groups [5]. Other advantages of paper-based biosensors include simple and fast production, easy disposal, biodegradability, portability, user-friendliness, low cost, and low waste in the environment [6,7].

Methods: In recent years, the overuse of antibiotics has caused more and more serious environmental pollution. The uncontrolled abuse of antibiotics makes bacteria produce resistance to antibiotics faster than the replacement rate of antibiotics themselves, leading to the emergence of super drug-resistant bacteria. Therefore, it is of great practical significance to establish a simple, rapid and sensitive method for the detection of antibiotics. By integrating natural nano-clay (Atta) and carbon dots (CDs), the real-time and rapid visual detection of tetracycline (TC) in the sample can be realized by chromaticity pick-up APP on smartphones. The nano-sensor can detect tetracycline in the concentration between 25 nM and 20 μM with the detection limit of 8.7 nM. The low detection limit coupled with good accuracy, sensitivity

and specificity meets the requirements for the detection of tetracycline in food. More importantly, the test paper and fluorescent stick-like nano-sensor are designed to detect tetracycline by polychromatic fluorescence changes [8]. A novel “turn-on” fluorescent sensor based on R-CDs was developed for the selective detection of Tetracyclines (TCs) and pH. The R-CDs with red emission were prepared via hydrothermal treatment using neutral red and thiourea as carbon source. Besides, the R-CDs showed a distinct pH-sensitive luminescence emission feature in the pH range of 6.0–8.0 with a pKa of 7.08 [9].

Results: When the TCs were directly mixed with CDs, the fluorescence quenching phenomenon appeared. Since different TCs exhibited different affinities for sensing elements, the sensor array displays a distinct fluorescence pattern of the fluorescence intensity variation (F0 − F)/F0 for each of these TCs, which is further analyzed by principal component analysis (PCA). The present fluorescent sensor array has the capacity to differentiate TCs at a low concentration of 1 μM. Meanwhile, quantitative detection with a lower limit (0.30 μM) for TCs could be achieved by applying a single element. Moreover, a high accuracy (100%) examination of unknown samples is acquired. Finally, the fluorescent sensor array performs well in distinguishing binary mixtures and could also recognize TCs in milk [10].

Conclusion: An important challenge in nanomaterial-based antibiotic biosensors is the practical application, such as on-site analysis of analytes for the real samples and complex environments. For this reason, all biosensing devices should eventually be suitable for the end-user. Unfortunately, so far, biosensor-related innovations are limited to the laboratory scale, and less attention has been paid to the end-users' needs. Therefore, effective technology is still highly desired, enabling the rapid production of large amounts of nanomaterial-based biosensors with high-quality specifications and relatively low cost. Such a technique is the prerequisite for the successful commercial application of any biosensing device. Future efforts should focus on developing multifunctional nanomaterials and making the antibiotic biosensors more robust [11].

Keywords: carbon dots (CDs), paper-based sensors, antibiotics, antimicrobial resistance (AMR), biocompatibilit

Recombinant expression of DT-Diaphorase enzyme: A new approach for activation of cancer chemotherapeutic prodrugs (Research Paper)

hamideh askari,[1] faeze khakbaz,[2] maryam zaboli,[3] masoud torkzade-mahani,[4,*]

1. Department of Biotechnology, Institute of Science, High Technology and Environmental Sciences, Graduate University of Advanced Technology, Kerman, Iran
2. Department of Nano Chemistry, Faculty of Chemistry, Shahid Bahonar University, Kerman, Iran.
3. department of chemistry, faculty of science, university of Birjand, Birjand, Iran
4. Department of Biotechnology, Institute of Science, High Technology and Environmental Sciences, Graduate University of Advanced Technology, Kerman, Iran

Introduction: DT-Diaphorase (flavin-containing enzyme) as a member of oxidoreductase family has been shown to have a role in activation of quinone-containing cancer chemotherapeutic prodrugs to their active form, as well as inactivation of a variety of xenobiotics involved in carcinogenesis and also has received wide attention as the key anodic enzyme mediating the electron transfer and electric energy generation in enzymatic biofuel cells (EBFCs). According to significant roles of this enzyme in many fields of biotechnology specially in cancer studies, biosensor design and in vitro diagnostic tests, we describe optimum recombinant expression conditions, characterization and application of a DT-Diaphorase enzyme.

Methods: The transformed recombinant plasmids to E. coli BL21 competent cells were used for protein expression. Recombinant histidine -tailed DTD enzyme was expressed in 10 mL LB medium containing 80 µ g/m L kanamycin at 37oC for 16 hours. Then the cells were collected by centrifugation at 1500 g for 10 minutes at 4oC and suspended in 4 mL of LB medium. The seeding was added to Terrific Broth (TB) medium to cell cultured reached an OD600 of about 0.1 and were incubated at 37oC with shaking at 180 rpm. When the cell cultures reached an OD600 0f 0.6, cells were incubated with IPTG (1mL, 1mM) in various temperatures (18, 25, 30 and 37oC) and times (5 and 10 hours). The bacterial cells were collected by centrifugation at 6000 rpm for 10 minutes at 4oC and were suspended in detergent lysis buffer. Several cycles sonication in ice bath was used for broken the bacterial cells walls. The supernatant was collected using centrifuge at 13000 rpm for 20 minutes at 4oC. The Ni-sepharose affinity and size exclusion chromatography were used for purification of prepared DTD enzyme. SDS –PAGE analysis, activity measurement (according to the absorption of formazan as a product of enzymatic reaction at 550 nm using

cary 50 UV-Vis spectrophotometer) and Bradford assay were used for study the enzyme properties.

Results: To obtain the best protein expression condition, two of the most important effective factors (incubation time and temperature) were optimized. The highest expression level of protein expression was examined by various factors such as single and broad 47 kDa band in SDS-PAGE analysis, high activity, and high enzyme concentration. According to obtained results, incubation of bacterial cells in 18oC for 5 hours can be the best condition for DTD expression.

Conclusion: DT-Diaphorase as an important enzyme in biotechnology such as early detection of cancer has attracted much attention. In this work, the optimized condition for DTD expression have been reported (incubation in 18oC for 5 hours). According to a colorimetric rout as a sensitive method for investigation the activity of prepared enzyme, the obtained DTD in the optimal conditions shows the activity as much as 10.76 units per 5 µL. A single and sharp 47kDa band in SDS-PAGE analysis is the other evidence for success enzyme expression.

Keywords: Enzyme expression, DT-Diaphorase

Reconstruction and repair of damaged axons in MS with the help of stem cells in the pulp of wisdom teeth and deciduous teeth (Review)

Saghar masoumi,[1,*]

1. khadije kobra highschool

Introduction: Multiple sclerosis (MS) is an inflammatory and autoimmune disease in which the myelin around axons in the brain and spinal cord is invaded and destroyed by the immune system. Over the past few decades, various therapeutic solutions have been proposed to solve this problem and one of them is the use of stem cells. The pulp of wisdom teeth and deciduous teeth is a source of stem cells. Unfortunately, people belive that these teeth have no special use and that's why they throw them away. So in this article I want to offer a cheaper way to treat MS with stem cells of these teeth and avoid them from being wasted.

Methods: In this review study, nearly fourty articles were reviewed from reputable sites such as: pubmed, connected papers, google scholar. Thirty seven articles were in English and three articles were in Persian. Among all of them ten articles were selected about MS, its treatment and dental pulp stem cells.

Results: Dental pulp stem cells have been tested in the treatment of neurological injuries such as: Alzheimer's, Parkinson's and optic nerve. In an experiment, researchers injected these cells into neural tissue of bird embryos. They could survive up to seven days and turned into nerve cells.

Conclusion: Dental pulp stem cells originate from (neural crest origin). That's the reason they can differentiate into nerve cells easily and quickly. They also have immunosuppressive properties. so their transplantation carries far fewer risks into the body. Due to the benefits of these stem cells, some banks can be set up to store wisdom and deciduous teeth. So we can use their stem cells to treat various diseases in the future.

Keywords: Multiple sclerosis, Stem cells, Dental pulp, Wisdom and deciduous teeth, Differentiation

Redroot pigweed Ethanolic Extract Toxicity on HDFa cells (Research Paper)

Hamideh Bakhshayeshan-Agdam,[1,*] Nastaran Sedghi ,[2] Seyed Yahya Salehi-Lisar ,[3] Majid Mahdavi ,[4]

1. Department of Plant Sciences, Faculty of Natural Sciences, University of Tabriz, Tabriz-5166616471, Iran
2. Department of Animal Sciences, Faculty of Natural Sciences, University of Tabriz, Tabriz-5166616471, Iran
3. Department of Plant Sciences, Faculty of Natural Sciences, University of Tabriz, Tabriz-5166616471, Iran
4. Department of Animal Sciences, Faculty of Natural Sciences, University of Tabriz, Tabriz-5166616471, Iran

Introduction: Cancer is currently one of the major causes of mortality and morbidity among humans. Extracts of plants have a potential source for treatments of Cancers, but the extracts toxicity on normal cells is a topic that today is receiving a lot of attention. Redroot pigweed (Amaranthus retroflexus L.) is a weed plant with well-known allelopathic effects. This plant has diverse therapeutic effects such as anti-leukemia properties due to specific biochemicals which involving in its allelopathic interaction as well. Results from MTT assay revealed that redroot pigweed ethanolic extract inhibits the viability and proliferation of NB4 cells, in a time- and dose-dependent manner. So that, 70% decline in viability of treated cells with 400 µg/ml of extract was observed after 72h.

Methods: In order to evaluate redroot pigweed ethanolic extract toxicity on normal cells (HDFa), normal cells treated with lower concentrations than IC50 for NB4 cells (160 µg/ml).

Results: Results from MTT assay showed that redroot pigweed ethanolic extract inhibits the viability and proliferation of HDFa cells in a time- and dose-dependent manner. At highest concentration of amaranth ethanolic extract (160 µg/ml), the viability percentage was more than 60%. Cell's viability in the culture media is declined over time due to influence various factors in the synthetic media, the same situation exists for HDFa cells. Hence, evaluation of apoptotic cells percentage using flowcytometry can provide reliable results for amaranth cytotoxicity.

Conclusion: Overally, this study demonstrates the potential of redroot pigweed ethanolic extract application as an anti-cancer drug for leukemia cancer treatment. Indeed, this investigation showed that the toxicity of the extract on normal cells is such that it could be used for safe treatment.

Keywords: Cancer, NB4 cells, HDFa cells, redroot pigweed, toxicity

Regenerate and repair of the skin by using of the hair follicle stem cells (Review)

Maryam Alizadeh,[1,*]

1. Student research Center, Baharestan 1 Education Office, Baharestan 1, Tehran, Iran

Introduction: Nowadays, the use of new therapies such as cell therapy has opened a new window for the treatment of the diseases. In cell therapy, embryonic and adult stem cells are used. Adult stem cells are present in several parts of the adult body, including the bone marrow and the adipose tissue. One of the tissues that has stem cells is the bulge area of the hair follicle. The hair follicle has a repository of stem cells that play a key role in the growth, repair and differentiation of the hair follicles. If the lower third of the follicle is cut off, the rest of the follicle can be repaired to make a new hair. Here, new epidermal cells originate from the bulge. In this study, skin regeneration and repair using hair follicle stem cells were investigated.

Methods: First, these cells must be properly directed to the keratinocyte line. The selection and purification of differentiated keratinocyte precursors is then performed by cell surface markers labeled with specific antibodies. In the next step, cytokines and external growth factors are used as a complement to the culture medium and final differentiation factors.

Results: In fact, the hair follicle is a viable option for adult stem cells due to its easy access and high-capacity differentiation potential. And if the above steps are done correctly, the hair follicle stem cells will differentiate into skin epithelial cells.

Conclusion: The use of hair follicle stem cells is a good option for the treatment of skin lesions and presents a bright future for the treatment of skin lesions before doctors and researchers.

Keywords: skin repair, cell therapy, hair follicles, stem cells

Relationship between Body Mass Index and Breast Cancer Stages
(Research Paper)

Ali Zarei,[1,*] Hossein Javid,[2] Hanieh Zarei,[3]

1. Iranian Academic Center for Education, Culture & Research (ACECR)-Fars Branch Institute for Human Genetics Research, Department of Human Genetics
2. Iranian Academic Center for Education, Culture & Research (ACECR)-Fars Branch Institute for Human Genetics Research, Department of Human Genetics
3. Physical Therapy Department, School of Rehabilitation Sciences, Shiraz University of Medical Sciences, Shiraz, Iran; Student Research Committee, Shiraz University of Medical Science, Shiraz, Iran.

Introduction: Introduction: Breast Cancer is a type of cancer that arises in the breast organ. Cancer happens when breast tissue cells continue to grow abnormally. Breast cancer rates are rising in developing Asian countries, especially Iran. Diagnosis of breast cancer in the early stages is one of the most essential issues in preventing the development of breast cancer.

Methods: Material and Method: Information on height, weight, stage of breast cancer, and body mass index at the time of diagnosis is available for 109 women undergoing early-stage breast cancer treatment in Nemazee hospital between the years 2017 to 2019. We examine the relationship of BMI to stage at diagnosis with t-tests.

Results: Results: Patients with a body mass index of 27kg/m2 or more have stages 3 and 4 of breast cancer, while patients with BMI below 27kg/m2 have stages 1 and 2 of breast cancer. Our result showed that a high body mass index is associated with stages 3 and 4 of breast cancer at diagnosis(P≥0.05).

Conclusion: Conclusion: High BMI and obesity are prognostic factors for the breast cancer and death of the patient. Early diagnosis of breast cancer is essential for the prevention and breast cancer treatment management.

Keywords: Breast Cancer-Body Mass Index-Prognosis-Obesity

Relationship between dietary vitamin B12 and folate, and esophageal squamous cell carcinoma (Research Paper)

Fateme Valipour Baboly,[1,*] Zeinab Sadat Moosavifard,[2]

1. BSc in Nursing, Department of Nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.
2. Department of Nursing, faculty of nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.

Introduction: Esophageal cancer is the second and third most common cancers in Iranian men and women after gastric cancer, respectively. It is estimated that about 5,800 Iranians die each year from esophageal cancer. In Iran, SCC cancer still accounts for more than 90% of gastric cancers, but adenocarcinoma-type esophageal cancer is gradually increasing. This study was performed to investigate the relationship between folate intake, vitamin B12 and the risk of squamous cell carcinoma of the esophagus (SCCE).

Methods: In this case-control study, the case group included 80 patients with SCCE in the main hospitals of Hormozgan province and the control group (which were matched with the case group in terms of age and sex) included 80 patients with acute diseases. And non-cancerous were in the same centers. Background data and physical activity were assessed by a written questionnaire. Nutrition data were collected with a feed frequency questionnaire, then folate and vitamin B12 levels were calculated using Nutritionist IV (N4).

Results: 38% of the subjects in the case group and 40% of the subjects in the control group were male. The mean age of the case group was 58 ± 18 years and the control group was 58 ± 17 years. The mean folate intake in the case group was 1.153 micrograms per day less than the control group. After adjusting for confounding variables, it was inversely associated with SCCE (odds ratio 0.03 and 95% confidence interval: 0.008 to 0.12). The relationship between B12 consumption and SCCE was not significant (P = 0.46).

Conclusion: Folate intake has a significant inverse relationship with the risk of SCCE. No relationship was found between B12 and SCCE. Therefore, people's diet should be planned to contain folate in the diet.

Keywords: dietary , vitamin B12 , folate, esophageal, carcinoma

Relationship between Helicobacter pylori infection and its violence with diet in Yazd (Research Paper)

Mostafa rahimi nasab,[1,*] Ruholla rahimi nasab,[2] Mohammad Javad Forouzani-Moghaddam,[3]

1. Bachelor of Biotechnology, Yazd University, Yazd, Iran
2. Bachelor of Biotechnology, Yazd University, Yazd, Iran
3. Msc of Food Microbiology, School of Paramedical, Iran University of Medical Sciences, Tehran, Iran

Introduction: Gastric cancer is the most common malignancy in Iran. Helicobacter pylori and some components of the diet are among the risk factors for this disease, but there are few studies on the relationship between these two factors in the world. The aim of this study was to investigate the relationship between Helicobacter pylori infection and its severity with diet in Yazd.

Methods: This study was a cross-sectional descriptive study. The samples were 98 people who underwent upper endoscopy in Yazd Gastroenterology and Liver Research Center. A questionnaire containing demographic information and a food frequency questionnaire for individuals was filled out and a sample of anther was sent for pathological examination. Data analysis was performed by non-parametric tests.

Results: The rate of Helicobacter pylori infection was 51.2% based on pathological examination (hematoxylin-eosin). Positive HP infection was inversely related to weekly consumption of fish (P = 0.008), green pepper (P = 0.015) and water (P = 0.02) and weekly consumption of tuna (P = 0.016) and tea (P = 0.052) was directly related. The severity of HP infection was inversely related to weekly consumption of fish (P = 0.002), green pepper (P = 0.049) and water (P = 0.002) and with weekly consumption of tuna (P = 0.015) and sugar (P = 0.047) was directly related.

Conclusion: The results indicate the possibility of the effect of some foods such as fish (except tuna), green pepper and water on HP and the severity of this infection. Due to the limitations of this study, more comprehensive and accurate studies are necessary to prove the findings and achieve more details.

Keywords: Helicobacter pylori, diet, Gastric cancer, Risk factors

Relationship between nutrition and gastric cancer (Review)

zeinab sadat moosavi fard,[1,*]

1. Department of Nursing, faculty of nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.

Introduction: Gastric cancer is the fourth most common cancer in the world and is the second leading cause of cancer mortality. The prevalence of this cancer is caused by cancer cells on the inner lining of the stomach and is classified as a multifactorial disease. Lifestyle, diet, hereditary and environmental factors are considered effective, although Helicobacter pylori infection is a very important factor in gastric cancer. The role of nutrition as the most important environmental factor in the incidence, control and prevention of gastric cancer is very important. The present study reviews previous studies to investigate several dietary factors and gastric cancer.

Methods: The present study is a kind of review study that has been done in order to link nutrition and gastric cancer. Search in databases such as Pubmed, Scopus, Google scholar and Science Direct with keywords such as gastric cancer, green tea, meatand prosses meat, vegetables and fruit, Helicobacter pylori in Time range 2007B 2019, 36 articles were found, and after deleting unrelated and non-original articles, 19 articles were included in the study.

Results: The risk of stomach cancer is reduced by consuming more fruits and vegetables and perhaps green tea. Consumption of processed meats, salt and salty foods, alcohol, hot tea, very hot foods, fried oils, high consumption of foods Containing pigments and preservatives is associated with an increased risk of gastric cancer. Evidence based on the concentration of nitrate in drinking water and gastric cancer has been observed. On the other hand, there is no clear evidence on how meat, fish, coffee, black tea and gastric cancer are related.

Conclusion: Nutritional factors such as consumption of processed meat, fried foods, salt, salty foods and insufficient consumption of fruits and vegetables are risk factors for gastric cancer, so to prevent gastric cancer, proper nutritional planning should be To be considered.

Keywords: gastric cancer, nutrition, relationship

Relationship Between Pregnancy Associated Plasma Protein and Gestational Diabetes (Review)

Mina Soleimani,[1,*] Fatemeh Mohebi,[2] Hanane Hamidi,[3]

1. Iran University of Medical Sciences, Tehran, Iran
2.
3. Khalkhal University

Introduction: GDM (Gestational diabetes mellitus) is the most common metabolic complication in pregnancy and is related to maternal and fetal mortality and morbidity. On this background, simple and effective detection strategy for GDM in the early pregnancy is needed. The pathophysiology of GDM takes place weeks to months before diagnosis and factors associated with this pathogenesis exist in blood before the clinical diagnosis of GDM. In GDM, the placenta endures changes such as increased hyper-vascularization and dysfunction of blood stream of the placental villi. PAPP-A (Pregnancy Associated Plasma Protein) is produced by the placental syncytiotrophoblast and commonly assess in prenatal screening at 11-14 weeks of gestation for prediction some aneuploidies such as chromosomal trisomy like 21. The aim of the present study was to assess whether serum PAPP-A concentrations can predict GDM or show improved value for predicting GDM when combined with maternal factors.

Methods: In this review article we comprehensively studied more than 20 article of PubMed/MEDLINE, Web of science from 2015 to 2021.

Results: 15 studies show that there is a significant relationship between PAPP-A and GDM and 5 studies didn't find anything significant. First trimester MoM level of PAAP-A marker was lower in women who later developed GDM 0/7(0/5-1/2) compared to women who remained norm glycemic throughout pregnancy 1/2 (0/8-1/6).

Conclusion: According to these studies we can conclude that women diagnosed with GDM have lower first trimester levels of PAPP-A than women who remain normoglycemic throughout pregnancy. Measurement of first trimester biomarker that represents the metabolic change may allow for early detection and management of GDM. This biomarker may use as indicators of the presence of abnormal glucose metabolism at the start of pregnancy and could aid in the identification of women at risk for GDM development

Keywords: Gestational diabetes, pregnancy associated plasma protein

Relationship between probiotics on type II diabetes mellitus: a meta-analysis (Review)

faezeh sarafraz,[1] Nazanin Zare,[2] Mohammad Javad Forouzani-Moghaddam,[3,*]

1. Msc of Food Microbiology, School of Paramedical, Iran University of Medical Sciences, Tehran, Iran
2. MSc of Pathogenic microbes, School of Science, Shahid Bahonar University, Kerman, Iran
3. Msc of Food Microbiology, School of Paramedical, Iran University of Medical Sciences, Tehran, Iran

Introduction: The purpose of the present study was to evaluate the efectiveness of probiotics on type II diabetes mel- litus (T2DM). The worldwide prevalence of type 2 diabetes mellitus (T2DM) is constantly increasing, and it has become a major concern, with several implications for public health, economy, and social well-being. It is well-known that several factors such as lifestyle, increased intake of fat and sugar-rich foods, and host genetics can lead to T2DM. Some recent studies have suggested that the composition of the intestinal microbiota can trigger T2DM.

Methods: We performed a comprehensive search on PubMed, Web of Science, China National Knowledge Infrastruc- ture, Chinese Scientifc Journal Databases, Wan Fang database and China biology medicine disc for relevant studies published before June 2019. Glycated hemoglobin A1c (HbA1c), homeostasis model assessment of insulin resistance (HOMA-IR) and fasting blood glucose (FBG) were used as indicators for T2DM. Inverse-variance weighted mean difer- ence (WMD) with 95% confdence interval (CI) was calculated for the mean HbA1c, FBG and HOMA-IR changes from baseline.

Results: 15 randomized controlled trials (RCT) with a total of 902 participants were included into the meta-analysis. Considering the clinical heterogeneity caused by variation of dosage and duration of probiotic treatment, random efects model was used to estimate the pooled WMD. Signifcantly greater reduction in HbA1c% (WMD=−0.24, 95% CI [−0.44, −0.04], p=0.02), FBG (WMD=−0.44 mmol/L, 95% CI [−0.74, −0.15], p=0.003) and HOMA-IR (WMD=−1.07, 95% CI [−1.58, −0.56], p<0.00001) were observed in probiotics treated group. Further sensitivity analysis verifed the reliability and stability of our results.

Conclusion: The results of our meta-analysis indicated that probiotics treatment may reduce HbA1c, FBG and insulin resistance level in T2DM patients. More clinical data and research into the mechanism of probiotics are

needed to clarify the role of probiotics in T2DM. Since then, considerable effort has been made to understand the link between the composition of intestinal microbiota and T2DM, as well as the role of probiotics in modulation of intestinal microbiota. This mini-review summarizes the major findings and discusses the close relationship between intestinal microbiota, probiotics, and T2DM.

Keywords: Type 2 diabetes . Gut microbiota . Probiotic . Chronic disease

Relationship between pulmonary function and anthropometric indices with different levels of physical activity in male employees (Research Paper)

Mohammad hosein aghidemand ,[1,*] Hadis Bayat ,[2]

1. Allameh Tabataba'i University
2. PhD student in Sports Physiology, Faculty of Humanities, Physical Education and Sports Sciences, Science and Research Branch University

Introduction: Background & Aims: Physical activity and lifestyle is one of the important and influential factors on human health. Pulmonary function is also directly related to a person's level of health. Therefore, the aim of the present study was to compare the relationship between pulmonary function and different levels of physical activity in office workers.

Methods: Methodology: A total of 154 available male employees participated in this study. First, demographic information was collected and recorded. The International Physical Activity Questionnaire (IPAQ) was used to determine their level of physical activity. Based on the results of the questionnaire, the level of physical activity of the subjects was classified into four levels of physical activity (low, medium, balanced, high). Then, pulmonary volumes and capacities were measured, including: rapid expiratory expiratory capacity (FVC), vital capacity test (VC), maximal voluntary ventilation (MVV) test using a spirometer. Then the body anthropometric indices including Body mass index (BMI), waist circumference (WC) and distance ratio Waist and hip (WHR) were measured and recorded. Also, ANOVA statistical test was used for intergroup comparison. All statistical analyzes were performed using SPSS software version 21. Body mass index (BMI), waist circumference (WC) and distance ratio Waist and hip (WHR) were measured and recorded. Also, ANOVA statistical test was used for intergroup comparison. All statistical analyzes were performed using SPSS software version 21.

Results: Results: The results of the present study showed that there was a significant difference between individuals with low and high levels of physical activity for BMI and WHR indices ($p < 0.05$). On the other hand, no significant difference was observed between subjects with different levels of physical activity for FVC, VC, MVV and WC levels ($p = 0.1$, $p = 0.5$, $p=0.32$, $p=0.41$).

Conclusion: Conclusion: High level of physical activity does not negatively affect pulmonary function and also the higher the level of physical activity of office workers, the levels of anthropometric indices are desirable and increase health among office workers.

Keywords: Physical activity, Office staff, Pulmonary function, Spirometry

Research on the effects of exosomes derived from liver cells in treatment of liver diseases (Review)

Niloofar Torkzadeh,[1,*] Mozhgan shirazi,[2]

1. Department of Biochemistry, Islamic Azad University, Falavarjan,Iran
2. Department of Biology, Scince and Reserch Branch, Islamic Azad University, Tehran, iran

Introduction: Extracellular vesicles derived from mesenchymal stem cells (MSC-EVs) have been widely reported as promising cell free products that show therapeutic effects of the parental cells but not their limitations. The most effective treatment for end stage liver fibrosis is currently liver transplantations, however, transplantation is limited by a shortage of donor organs, surgical complications, immunological rejection, and high medical costs. Recently mesenchymal stem cell (MSC) therapy has been suggested as an effective alternate approach for the treatment of hepatic diseases.

Methods: We reviewed about 22 articles were conducted from 2017 to 2021 in the world and Iran. We searched some key words such as mesenchymal stromal cells, exosome, liver cirrhosis, immune modulation, trophic factors, liver fibrosis in Science direct, Elsevier, PubMed and SID.

Results: MSCs have the potential to differentiate into hepatocytes, and therapeutic value exists in their immunomodulatory properties and secretion of trophic factors, such as growth factors and cytokines. In addition, MSCs can suppress inflammatory responses, reduce hepatocyte apoptosis, increase hepatocyte, regeneration, regress liver fibrosis and enhance liver functionality. Exosomes are extracellular vesicles with diameters ranging from 30 to 150nm, which contain several donor cell associated proteins as well as mRNA, miRNA, and lipids and coordinate multiple physiological and pathological functions through horizontal communication between cell. Almost all types of liver cells, such as hepatocytes and kupffer cells, are exosome releasing and /or exosome targeted cells. Exosomes secreted by liver cells play an important role in regulating general physiological functions and also participate in the onset and development of (liver) diseases, including liver cancer, liver injury, liver fibrosis and viral hepatitis. Liver cell derived exosomes carry liver cell specific proteins and miRNAs, which can be used as diagnostic biomarkers and treatment targets of liver disease. Researchers have demonstrated that miRNA_122 loaded in exosomes derived from mesenchymal stem cells (MSCs) can inhibit the activation and proliferation of primary HSCs, and continued treatment for 4 weeks using this method can improve ccl4 induced liver fibrosis in mice. Ohara et al. demonstrated that amniotic mesenchymal stem cell derived extracellular vesicles in primary cell culture can suppress the activation of kupffer cells and HSCs and can

improve ccl4 induced liver fibrosis. Exosome derived from human umbilical cord mesenchymal stem cells (HUC_MSCs) also reduce fibrosis by inhibiting the expression of collagen and TGF_β1 in vivo. In addition, MSC derived exosomes suppress liver fibrosis by improving liver function and inhibiting inflammation and HSC activation. In HCV induced fibrosis, HCV replicating hepatocytes transfer miRNA192 to HSCs through exosomes, activating HSCs and inducing their trans differentiation into myofibroblasts. This suggests that exosomal miR_192 is major regulator and potential therapeutic target in liver fibrosis induced by HCV.

Conclusion: This review discusses the functions of exosome derived from different liver cells and provides novel insights based on the latest developments regarding the roles of exosome in the diagnosis and treatment of liver diseases. We also present several outstanding risks, including

Keywords: Exosome, liver cirrhosis, immune modulation, trophic factors, Extracellular vesicles

Respiratory Virus Receptors: Diversity, Identity, and Therapeutics (Review)

Farzane Behnezhad,[1] Najmeh Parhizgari,[2] Talat Mokhtari-Azad,[3] Vahid Salimi,[4,*]

1. Tehran University of Medical Science
2. Tehran University of Medical Science
3. Tehran University of Medical Science
4. Tehran University of Medical Science

Introduction: Viruses are one of the most common causes of respiratory tract infection in humans worldwide. Indeed, the ongoing severe acute viral respiratory diseases are a major threat to global health that highlights the need for effective therapeutics for viral respiratory infections. One of the promising potential targets for antiviral therapy is cellular receptors for viral entry that play a key role in the viral life cycle and pathogenesis. The present study aims to have an overview of viral respiratory receptors and their roles in host range, pathogenesis, and therapeutic targets to fight the disease and save lives.

Methods: This study was a narrative review performed in 2021 to investigate viral respiratory receptors and antiviral therapeutic strategies. We searched six databases including PubMed, Scopus, Science Direct, Web of Science, and Google scholar to determine the related documents on the main objective of the study. In this review, we briefly summarized important respiratory viruses cell receptors including influenza virus, human respiratory syncytial virus, coronavirus, human metapneumovirus, human Parainfluenza virus, human adenovirus, and human rhinovirus and their receptors to introduce the known receptor for each virus and the potential preventives or therapeutics related to these targets.

Results: A review of current studies revealed that virus-receptor interactions are essential for the successful infection of respiratory viruses by invading host cells. viruses usually use specific cell receptors, however, many of them use common viral receptors such as Heparan sulfate proteoglycans (HSPG), widely expressed by most cell types, that are broadly used by a range of respiratory viruses, to bind to the cell surface. Designing antiviral compounds to prevent HS binding is one of the targets for the design of future antiviral therapies. Moreover, several viruses like influenza viruses, coronaviruses, and adenoviruses utilize sialic acids as cellular entry receptors. Sialic acid receptors widespread distribute in many different cell types like the entire respiratory tract in animals and humans that play crucial roles in the ability to jump species and adapt to the human host. This information will help to

develop more important targeted to prevent viruses cell entry by blocking their receptors.

Conclusion: An in-depth understanding of the mechanisms of viral infection, receptors play an important key in host susceptibility to viruses. Therefore, new antiviral therapeutics are developed by identification of virus interactions with host cells in viral pathogenesis and finding novel anti respiratory virus targets.

Keywords: Viral Receptors, Respiratory Viruses, Viral attachment, Cellular adhesion molecules

Response surface method optimization of photodynamic therapy conditions for treatment of skin cancer using zinc phthalocyanine-nanoemulsions (Research Paper)

Fatemeh Saeedi,[1,*] Malahat Rezaee,[2] Mahnoosh Fatemi,[3] Fereshte Ghandehari,[4] Ramesh Monajemi,[5]

1. Department of Biochemistry, Falavarjan Branch, Islamic Azad University, Isfahan, Iran
2. Department of Biochemistry, Falavarjan Branch, Islamic Azad University, Isfahan, Iran
3.
4. Department of Microbiology, Falavarjan Branch, Islamic Azad University, Isfahan, Iran
5.

Introduction: Melanoma is the most dangerous form of skin cancer, with a steeply rising incidence and a poor prognosis in its advanced stages. Melanoma is much less common than the other types but much more likely to invade nearby tissue and spread to other parts of the body. Since melanoma is highly resistant to traditional chemotherapy and radiotherapy, various alternative treatments are being investigated to develop melanoma therapy. Photodynamic therapy (PDT) has been proposed as an effective modality for melanoma therapy, superior to traditional forms of therapy because of its noninvasiveness, fewer side effects, negligible drug resistance, and low systemic toxicity. PDT employs a photosensitizer (PS) and visible light in the presence of oxygen, leading to production of cytotoxic reactive oxygen species, which can damage the cellular organelles and cause cell death. The aim of this study was to optimize phothodynamic therapy conditions of zinc phthalocyanine as a photosensitizer incorporated in a nanoemulsion system to achieve the lowest viability of skin cancer cell line.

Methods: Response surface methodology (RSM) was employed to study the effect of the drug dose (10, 20, 40 and 80 µg/ml) and laser dose (1.25, 2.5, 5 and 20 J/cm3) as independent factors on viability percentage of melanoma cell line, as response. The incubation time was hold constant at 4 hr. The melanoma cancer cell line was B16F0 and the cell viability was determined using MTT assay. A three-factor central composite rotatable design (CCRD) was used to determine the effect of the factors on the response. Experimental runs were generated by using Design-Expert version 10 (State-Ease Inc., Statistics Made Easy, Minneapolis, MN, USA). Experimental data was analyzed by multiple regressions to fit all the experimental data to the partial third order polynomial equation. An analysis of variance (ANOVA) and R2 (coefficient of determination) statistic was carried out to evaluate significant differences between independent variables.

Results: The results showed that the experimental data could be sufficiently fitted into a third-order polynomial model with multiple regression coefficients (R2) and adjusted R2 of 0.88 and 0.76, respectively. The F-value of the model in ANOVA was 7.36 implied that the model was significant. The non-significant lack of fit (P-value = 0.074) indicated that the partial cubic polynomial model was an appropriate model for predicting the data. Among the linear, quadratic, cubic and interaction terms, the quadratic term of drug concentration was the most effective factors (P-value = 0.003). In addition, PRESS was 1700.02, and adequate precision was 6.588, which confirm accuracy of the model. The optimum photodynamic conditions were drug concentration of 78.28 µg/ml and laser dose of 17.22 J/cm3. The achieved viability was 10% for the cancer cell line.

Conclusion: The results showed that RSM was efficient in modeling and optimizing photodynamic parameters, and zinc phthalocyanine-nanoemulsions had significant effects on reduction of viability percentage of skin cancer cell line.

Keywords: Response surface methodology, Photodynamic therapy, Melanoma, Zn phthalocyanine, Nanoemulsions,

Rheology evaluation of Gelatin/ Alginate/ Laponite nanocomposite hydrogel for Tissue Engineering applications (Research Paper)

Faezeh Shahedi Aliabad,[1] Elnaz Tamjid,[2,*]

1. Department of Nanobiotechnology, Faculty of Biological Sciences, Tarbiat Modares University, Tehran, Iran
2. Department of Nanobiotechnology, Faculty of Biological Sciences, Tarbiat Modares University, Tehran, Iran

Introduction: Gelatin is a natural polymer synthesizing from partial denaturation of Collagen which is biocompatible, biodegradable, and inexpensive with cell attachment motifs. In contrast, Sodium alginate is a natural polymer extracted from brown algae and doesn't have cell attachment domains. Despite the fast degradation of Gelatin in physiological environments, mammalian cells are not able to break sodium alginate down. Therefore, incorporating a proper ratio of these polymers could be desirable for tissue regeneration but they don't have enough mechanical and rheological properties. Furthermore, laponite platelets are synthetic disk-like nanomaterials with 25 nm diameter and 0.95 nm thickness which Adding them as nanofillers improve mechanical and rheological properties of composites. Tissue engineering aims to construct biocompatible scaffolds as mechanical and chemical support for cell growth, proliferation, and adhesion. Bioprinting is an attractive manufacturing method to construct scaffolds and is promising for tissue regeneration. The studied hydrogels in this research were all injectable with good rheological characteristics thus they are promising for use as bioink in 3D bioprinting. In this study, laponite, gelatin, and alginate were combined and viscosity and viscoelastic behavior of unset and set gels were performed respectively.

Methods: Three hydrogels containing 4% Gelatin, 2% Sodium alginate, and (0-2%) w/v Laponite were produced through stirring at 55°C. CaCl2 solution which crosslinks alginate chains is used as the crosslinker of the hydrogels. Unset hydrogels (before crosslinking with CaCl2) and crosslinked samples were used for viscosity and viscoelastic analysis respectively. Hydrogel solutions were cast in 24-well plate and crosslinked with immerging in 100 mM CaCl2 thus disk shape samples with 14 mm diameter and 4 mm height were created. All samples were kept at 4°C for 10 days then the rheological characterizations were performed using an Anton Paar MCR-502 Modular Compact Rheometer. Analysis was conducted using a parallel plate geometry with 25 mm diameter and 1 mm gap size at room temperature (25°C). Viscosity measurements were performed in the shear rate range of 0.01 to 1000 1/s. In addition, amplitude sweep tests were carried out to estimate viscoelasticity and mechanical characterization of crosslinked hydrogels. First, strain sweep tests were conducted at a constant frequency of 10 rad 1/s with

a shear strain range of 0.01-100%. Based on the results, linear viscoelasticity (LVE) range was defined for gels so frequency sweep test performed in strain rate of 0.1% with frequency from 0.1 to 628 rad/s.

Results: Based on the results, all samples were injectable (shear thinning) which means the viscosity of the samples decreased through increasing shear rate progressively. physical cross-linking influences on viscosity and mechanical profile. incorporation of 1% (w/v) Laponite into the network increased viscosity, storage (G') and loss modulus (G") of the nanocomposites Because negative surfaces and positive edges of laponite platelets could interact with gelatin and alginate respectively. In other words, adding laponite (1% w/v) enhanced the viscosity of the hydrogel from 255 to 320 Pa.s but nanocomposites with 2% laponite due to aggregation of platelets represented less viscosity (222 Pa.s). G' was greater than G" for all samples which shows the solid behavior of each hydrogel. Further, G', G" and consequently mechanical stability of nanocomposites improved by the addition of laponite platelets into the structure.

Conclusion: In conclusion, in this study, a nanocomposite based on gelatin, alginate, and laponite was fabricated and rheological tests were conducted. Incorporating Laponite into the network develops electrostatic interactions with polymers so the viscosity profile improves. A strong shear-thinning profile and solid-like behavior guarantee printability of the hydrogels and shape-retaining after printing. addition of 1% Laponite improved shear-thinning and solid-like behavior of the hydrogel strongly.

Keywords: Gelatin; Alginate; Laponite; Hydrogel; Rheological characteristics

risk factors during pregnancy and preterm birth (Research Paper)

nasim sadat pajohanfar,[1,*] Roghaieh Rahmani bilandi,[2] Reza Esmaeili,[3] Fatemeh Mohammadzade,[4] Javad Sadeghinasab,[5]

1. Department of Midwifery, Faculty of Medicine, Student workgroup of Social Determinants of Health Research Center, Gonabad University of Medical Sciences, Gonabad, Iran
2. Assistant professor, Department of Midwifery, Social Development and Health Promotion Research Center, Faculty of Medicine, Gonabad University of Medical Sciences, Gonabad, Iran.
3. Department of Public Health, School of Health, Social Determinants of Health Research Center, Gonabad University of Medical Sciences, Gonabad, Iran
4. Department of Biostatistics, School of Medicine, Gonabad University of Medical Sciences, Khorasan Razavi, Iran
5. Department of pediatrics, faculty of Medicine, Gonabad University of medical science, Gonabad, Iran

Introduction: Premature birth is the most common cause of neonatal mortality and childhood disability, occurring in most cases without a known medical cause, and is an obstetrics complication with complex causes. It is necessary to identify the reasons of preterm birth to predict it and decrease amount of morbidity and mortality of mothers and their infants.

Methods: the study was performed on 7747 cases of mothers who gave birth with in 2016-2017 . 2000 of them which have not included criteria so they excluded from the study. we used a researcher-made checklist based on scientific texts and articles to generate information of their pregnancies and births.The final checklist data was entered in SPSS software version 16. .Logistic regression model was used to determine the factors associated with preterm birth.

Results: we realized that there are significant associations between some risk factors during pregnancy and preterm birth. maternal age older than 35 years old has a significant association with preterm birth ($p=0.001$). Multiple pregnancies were associated with preterm delivery($p<0.001$). Preterm births were increased in mothers who had diabetes pregnancy ($p<0.001$). there is a significant association between multi-parity and preterm birth ($p=0.01$).

Conclusion: Maternal age, multiple pregnancy, disease and parity are associated with preterm birth ; thus, identity and prediction preterm delivery to prevent mortality and morbidity mothers and infants are important.

Keywords: preterm birth, risk factor, pregnancy

Role of Malondialdehyde as an oxidative stress biomarker in pregnancy complications (Review)

Fatemeh Ranjbar,[1,*]

1.

Introduction: Pregnancy is well-known to increase the oxidative stress, a phenomenon generated by a normal systemic inflammatory response, which results in high amounts of circulating reactive oxygen species (ROS). The major source of ROS during pregnancy is the central organ that regulates this condition, i.e. the placenta. Pregnancy complications including pre-eclampsia, gestational diabetes mellitus, preterm birth, and intrauterine growth restriction can cause acute and chronic health problems for the mother and fetus. Current methods of predicting pregnancy complications are limited and although a large number of factors are associated with disease progression, few biomarkers have been used to aid in disease diagnosis early in gestation. Malondialdehyde (MDA) is formed as a result of lipid peroxidation of polyunsaturated fatty acids which is commonly used to indicate lipid peroxidation and oxidative stress. In this article role of MDA as a biomarker used in the prediction or diagnosis of pregnancy disorders has been reviewed.

Methods: This article reviewed several articles published from 2015 to 2021 and available in PubMed in English. “Oxidative stress Biomarkers”, “Malondialdehyde”, and “Pregnancy Complications” were searched individually and in combination as keywords to find most related articles.

Results: MDA levels in second trimester women have been shown to be similar in the amniotic fluid of healthy control and pre-eclamptic women. In contrast women with pregnancy induced hypertension were found to have lower levels of MDA within amniotic fluid compared with controls. several studies have found elevated levels of MDA in serum/plasma of women with pregnancy disorders. Karowicz-Bilinska, demonstrated elevated serum MDA levels in women with IUGR. Pathak et al. similarly demonstrated that maternal blood MDA levels are increased at birth in women with preterm deliveries compared with women at full term.

Conclusion: Markers of oxidative stress are frequently reported as being increased in biological fluids of women with one or more of the above pregnancy complications. Many of the studies performed have focused on preeclampsia, but it is likely that an increase in any of the markers of oxidative stress would also be increased in a number of pregnancy complications. MDA in blood may prove to be a useful indicator of adversity during pregnancy; however, studies have highlighted some shortcomings in analyzing this

biomarker, most notably because MDA is a specific measure of lipid peroxidation and the most commonly used thiobarbituric acid reactive substance assay is not highly specific for MDA. As such, further studies need to be performed to investigate suitability of this marker and to determine how useful it would be in a diagnostic setting. The establishment of viable predictive biomarkers of pregnancy disorders may allow for the use of prophylactic treatment options while diagnostic markers may prove useful for the determination of individualized treatment strategies.

Keywords: Oxidative stress Biomarkers, Malondialdehyde, Pregnancy Complications

SARS-CoV-2 vaccines are now being developed in order to break the transmission cycle (Review)

Seyed Amir Mohammad Seyed Mirzajani,[1] Seyed Reza Mohebbi,[2,*] Seyed Masoud Hosseini,[3] Piruz Shadbash,[4] Mahsa Saeedi Niasar,[5] Hamid Asadzadeh-Aghdaei,[6]

1. Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences
2. Research Center for Gastroenterology and Liver Diseases, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
4. Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences
5. Research Center for Gastroenterology and Liver Diseases, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
6. Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Introduction: The coronavirus disease 2019 (COVID-19) pandemic is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was initially detected in late 2019 in China. Since the discovery of the SARS-CoV-2 virus and its genome, the scientific community has put up an extraordinary effort that has resulted in the creation of over 300 vaccine candidates. Several of these vaccines have received emergency approval. The elderly and those with comorbidities are the most vulnerable to severe coronavirus disease 2019 (COVID-19). A safe and efficient vaccine might protect these populations in two ways: direct protection, in which high-risk groups are immunized to avoid disease, and indirect protection, in which those who are in contact with high-risk people are vaccinated to minimize transmission.

Methods: In this study, we give a summary of the vaccine's efficiency as assessed by recent SARS-CoV-2 vaccination trials, as well as some data about how it cuts off the transmission cycle and protects individuals from developing severe illness.

Results: Although these last two years have been tough for everyone, these years witnessed the development and testing of several vaccines against the

severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), with some vaccines reportedly having more than 90% efficiency against COVID-19 in clinical trials. This extraordinary accomplishment comes at a time when COVID-19 cases are at their highest daily numbers around the world.

Conclusion: COVID-19 has quickly spread around the world, posing significant health, economic, environmental, and social concerns to the whole human population. The global economy is being seriously disrupted by the coronavirus pandemic. Almost every country is attempting to limit the spread of the disease by testing and treating patients, quarantining suspects via interaction monitoring, preventing big meetings, and maintaining total or partial curfew, among other efforts. Controlling the source of disease, cutting off the transmission cycle, and using current medicines and vaccines to prevent disease progression are all critical at this time. Existing evidence suggests that novel vaccine candidates might be useful in protecting people, especially in preventing the development of severe cases and hospitalization, but still, there are investigations that should be done on the efficacy of the vaccines against new variants that emerged recently. However, evidence shows, vaccines can reduce death rates and minimize the development of severe cases.

Keywords: SARS-CoV-2, COVID-19, vaccine, transmission

SARS-CoV-2: From the pathogenesis to potential anti-viral treatments (Review)

Peyman Kheirandish Zarandi,[1] Mohammad Reza Zinatizadeh,[2,*] Maryam Zinatizadeh,[3] Mohammad Hadi Yousefi,[4] Nima Rezaei,[5]

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Introduction: Introduction: The world is witnessing the spread of one of the members of Coronaviruses (CoVs) family, called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the 21st century. Considering the short time spent after its prevalence, limited information is known about the effect of the virus mechanism on different organs of the body; meanwhile the lack of specific treatment and vaccine for this virus has exposed millions of people to a big challenge. Areas covered: The review article aims to describe the general and particular characteristics of CoVs, their classification, genome structure, host cell infection, cytokine storm, anti-viral treatments, and inhibition of COVID-19-related ER-mitochondrial stress. In addition, it refers to drugs such as Chloroquine/Hydroxychloroquine, Lopinavir/Ritonavir, darunavir, ribavirin, remdesivir, and favipiravir, which have undergone clinical trials for coronavirus disease 2019 (COVID-19) treatment. This analysis was derived from an extensive scientific literature search including Pubmed, ScienceDirect, and Google Scholar performed. Expert opinion: The effectiveness rate and complications of these drugs can reveal new insights into the potential therapeutic goals for the disease. Moreover, lifestyle change can effectively prevent SARS-CoV-2 infection.

Methods: Introduction: The world is witnessing the spread of one of the members of Coronaviruses (CoVs) family, called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the 21st century. Considering the short time spent after its prevalence, limited information is known about the effect of the virus mechanism on different organs of the body; meanwhile the lack of specific treatment and vaccine for this virus has exposed millions of people to a big challenge. Areas covered: The review article aims to describe the general and particular characteristics of CoVs, their classification, genome structure, host cell infection, cytokine storm, anti-viral treatments, and inhibition of COVID-19-related ER-mitochondrial stress. In addition, it refers to drugs such as Chloroquine/Hydroxychloroquine, Lopinavir/Ritonavir, darunavir, ribavirin, remdesivir, and favipiravir, which have undergone clinical trials for coronavirus disease 2019 (COVID-19) treatment. This analysis was derived from an extensive scientific literature search including Pubmed,

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Conclusion: Introduction: The world is witnessing the spread of one of the members of Coronaviruses (CoVs) family, called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the 21st century. Considering the short time spent after its prevalence, limited information is known about the effect of the virus mechanism on different organs of the body; meanwhile the lack of specific treatment and vaccine for this virus has exposed millions of people to a big challenge. Areas covered: The review article aims to describe the general and particular characteristics of CoVs, their classification, genome structure, host cell infection, cytokine storm, anti-viral treatments, and inhibition of COVID-19-related ER-mitochondrial stress. In addition, it refers to drugs such as Chloroquine/Hydroxychloroquine, Lopinavir/Ritonavir, darunavir, ribavirin, remdesivir, and favipiravir, which have undergone clinical trials for coronavirus disease 2019 (COVID-19) treatment. This analysis was derived from an extensive scientific literature search including Pubmed, ScienceDirect, and Google Scholar performed. Expert opinion: The effectiveness rate and complications of these drugs can reveal new insights into the potential therapeutic goals for the disease. Moreover, lifestyle change can effectively prevent SARS-CoV-2 infection.

Keywords: Anti-viral treatments Cytokine storm MERS Pathogenesis SARS-CoV-2 SARS

Signaling pathways affecting MDR1 drug resistance (Review)

Nayereh Abdali,[1,*] Tahereh Abdali,[2]

1. 1* MSc of Medical Biotechnology, Faculty of advance Technologies, Shahrekord University of Medical Sciences, Shahrekord, Iran
2. MSc student in Plant Systematics, Yasouj University, Yasouj, Iran

Introduction: One of the problems of cancer patients is drug resistance. Several mechanisms are involved in the development of drug resistance, such as drug withdrawal from the ATP-dependent pump. P-gp is the most common family of ABC pumps that are encoded by the MDR1 gene and is the most important cause of drug resistance. Signaling pathways affect various biological factors in the body and the cell. Therefore, one of their goals could be MDR1 drug resistance pumps, which are regulated by the signaling pathways of this pump.

Methods: This is a review study Collected by reviewing articles related to the Signaling pathway and its effect on drug resistance MDR1 with the keywords "MDR1" OR "signaling pathway" and "P-gp" OR "signaling pathway" from 2017 onwards, from Google Scholar and Pubmed it has been compiled and written. 52 articles were collected, that of these 7 articles were excluded because of lack of subject relevance and only 45 studies were used. The inclusion criteria were all articles that examined the effect of different signaling pathways on MDR1 drug resistance.

Results: Different studies have shown that Numerous signaling pathways affect the performance regulation of MDR1 drug resistance pumps. VEGF, PI3k/AKT, FGFR, NF-KB, wnt, Raf-MAPK, MEK /ERK, JAK2/STAT3, MAPK, PXR, FZDZ/wnt, TGFB, Cjun-jNK are among the most important signaling pathways. that can reduce or increase MDR1 activity and expression.

Conclusion: Multiple signaling pathways affect drug resistance as a major challenge in the treatment of cancer patients. The MDR1 pump can be regulated to signaling pathways that have a reducing effect on it, such as the ERK signaling pathway, reducing its expression. As a result, treatment failure and drug resistance in cancer patients are reduced and the effectiveness of chemotherapy drugs is increased.

Keywords: MDR1, Drug resistance, Signaling pathway

Signaling Pathways Governing Endometrial Cancer Stem Cells Behavior (Review)

Maryam Farzaneh,[1,*]

1. Fertility, Infertility and Perinatology Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Introduction: Endometrial cancer is the most gynecological malignancy in the female genital tract. Endometrial cancer stem cells (ECSC) are a small population of cancer cells that represent a crucial role in the metastasis of endometrial cancer cells to other organs in the body. ECSC can proliferate and give rise to mature cancer cells, which are found to participate in the aggressiveness of metastatic lesions. Therefore, targeting ECSC can be a valuable strategy for drug development against the metastasis of endometrial cancer.

Methods: Previous studies have demonstrated that several signaling pathways, including Wnt, mTOR, EGFR, NOTCH, STAT3, VEGF, and SHH show modest effects and regulate the growth, epithelial-to-mesenchymal transition (EMT), and tumorigenesis of ECSC. miRNAs also play an important role in ECSC self-renewal, progression, and drug resistance.

Results: Hence, targeting these pathways might be a novel therapeutic approach for endometrial cancer diagnosis and therapy.

Conclusion: This mini-review aims to characterize the main signaling pathways involved in the stimulation of ECSCs proliferation and tumorigenesis.

Keywords: Endometrial cancer; Endometrial cancer stem cells; Signaling pathways; miRNAs; Metastasis

Silymarin: An antioxidant in Skin Cancer treatments (Review)

Khatere Sadeqzade,[1,*]

1. Mashhad university of medical sciences

Introduction: Skin cancer is the most common type of cancer, and its incidence has gradually increased in recent years. It is characterized by aberrant cell growth with a potential to invade or spread elsewhere in the body, which involves the complex process of carcinogenesis. Ultraviolet (UV) exposure is one of the main factors inducing skin cancer, and cutaneous cells may be damaged directly by UV radiation or indirectly by UV-mediated reactive oxygen species (ROS) overproduction. However, the role of ROS in skin cancer has not been completely clarified. An elevated oxidative status has been associated with melanoma. Oxidative stress is one of the key players in skin carcinogenesis, and therefore identifying nontoxic strong antioxidants to prevent skin cancer is an important area of research. Silymarin, a plant flavonoid isolated from the seeds of milk thistle (Silybum marianum), has been shown to have chemo preventive effects against chemical carcinogenesis as well as photo carcinogenesis in various animal tumor models. The aim of this study was reviewing recent publications evaluating Silymarin as an antioxidant in Skin Cancer treatments.

Methods: In order to find relevant studies to the research question, an electronic search with time (recent five years, up to 2021) and language (English) restrictions was conducted using PubMed. Most recent studies including case control studies, original research and review articles were selected. Analysis was done and data were synthesized and compiled in a sequential and presentable paradigm.

Results: Wide range of in vivo mechanistic studies indicated that silymarin possesses antioxidant, anti-inflammatory and immunomodulatory properties which may lead to the prevention of skin cancer in in vivo animal models. both animal and cell culture studies have shown that silymarin, a naturally occurring polyphenolic flavonoid antioxidant, exhibits preventive and anticancer effects against skin cancer. For example, silymarin strongly prevents both photo carcinogenesis and skin tumor promotion in mice, in part, by scavenging free radicals and reactive oxygen species and strengthening the antioxidant system. It also has been reported silymarin has an effect by inhibiting endogenous tumor promoter tumor necrosis factor α in mouse skin, a central mediator in skin tumor promotion. Furthermore, silymarin effectively modulates cell-cycle regulators and check points toward inhibition of proliferation, and growth arrest in G0-G1 and G2-M phases of the cell cycle.

Conclusion: Thus, the available experimental information and due to its mechanism-based chemo preventive and anticancer effects in experimental models, silymarin is an important candidate for the prevention and/or therapy of skin cancer, as well as other cancers of epithelial origin in humans. Moreover, silymarin may favorably supplement sunscreen protection and provide additional anti-photocarcinogenic protection.

Keywords: Silymarin, Antioxidant, Skin Cancer

Simultaneous Determination of Eight Sulfonamides and Trimethoprim Antibiotics Residues in Yogurt Samples by SPE clean-up and UHPLC-MS-MS (Research Paper)

Sara Kheirandish,[1] Shokoufeh Goudarzi,[2] Maryam Amirahmadi,[3] Shiva Ghareghani,[4] Bahram Daraei,[5] Mahmoud Ghazi-Khansari,[6,*]

1. Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
2. Food and Drug Reference Control Laboratories, Food and Drug Organization, MOH & ME, Tehran, Iran
3. Food and Drug Reference Control Laboratories, Food and Drug Laboratory Research Center, Food and Drug Organization, MOH & ME, Tehran, Iran
4. Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
5. Department of Toxicology and Pharmacology, School of Pharmacy, Shahid Beheshti University of Medical Science, Tehran, Iran
6. Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Introduction: Mismanagement of antibiotic drugs in livestock is the main source of antimicrobial residues in foodstuff. The transmission of antibiotic residues via foods of animal origin to humans can be able to antibiotic resistance as one of the most serious global public health problems. The present study aimed to develop and validate a sensitive and selective method to determine antibiotic residues of eight sulfonamides and trimethoprim in low-fat yogurt samples using Ultra-High-Performance Chromatography coupled to Tandem Mass Spectrometry (UHPLC-MS-MS) based on Solid-Phase Extraction (SPE).

Methods: HPLC parameters were optimized utilizing positive mode and multiple reaction monitoring (MRM) method. The separation was done on the C18 column using reverse-phase and Electrospray Ionization in positive mode (ESI+).

Results: The mean recovery and range of relative standard deviation (RSD) were obtained from 96.4-116.5% and 0.2-19.0%, respectively. The coefficient of determination (R2) was ≥ 0.9964 in the range of 10-200 ng/g. Limit of quantification (LOQ) and limit of detection (LOD) was obtained 10 and 3.3 ng/g, respectively.

Conclusion: A sensitive and selective method was developed for the analysis of 9 antibiotics in 34 low-fat yogurt samples. The RSD ≤ 20% for 8 antibiotics

showed the precision and accuracy of the validated method that could be applied to determine other antibiotics residues in milk and cheese.

Keywords: Antibiotic residue, Sulfonamide, Trimethoprim, Yogurt, UHPLC-MS-MS

Simvastatin prevents morphine-induced tolerance and dependence in mice (Research Paper)

nasim sadat pajohanfar,[1,*] bahareh amin,[2]

1. Department of Midwifery, School of Nursing, Sabzevar University of Medical Sciences, Sabzevar, Iran
2. Cellular and Molecular Research Center, Department of Physiology and Pharmacology, Faculty of Medicine, Sabzevar University of Medical Sciences, Sabzevar, Iran

Introduction: Tolerance to analgesic effects of opioids and dependence to them are main concerns in the treatment of chronic pain conditions, limiting clinical application of these drugs. This study aimed to evaluate the effect of simvastatin on the morphine-induced tolerance and dependence in mice.

Methods: For this purpose, mice were treated with either daily morphine (20 mg/kg, s.c.) alone, or in combination with simvastatin (2.5, 5 and 10 mg/kg, i.p.), for 9 continuous days. Antinociceptive effect of morphine was assessed through measuring latency time withdrawal of paw exposed to thermal stimulus, in the hot plate test. Naloxone-precipitated morphine withdrawal (5 mg/kg, i.p.), was used for dependence evaluation. Changes in brain gene expression levels of induced nitric oxide synthase (iNOS), astroglia marker, glial fibrillary acidic protein (GFAP), ionized calcium-binding protein (Iba1) a microglia activation marker, a pro-inflammatory mediator and tumor necrosis alpha (TNF-α) were measured after withdrawal by real-time polymerase chain reaction (RT-PCR).

Results: Behavioral tests indicated that latency time increased after morphine treatment in the hot plate test. However, this effect decreased on day 7, demonstrating tolerance to antinociceptive effect of morphine. Reduced anti-nociceptive effect of morphine was returned in animals treated with simvastatin (5 and 10 mg/kg) in combination with morphine. Simvastatin (5 and 10 mg/kg) attenuated morphine dependence as indicated by a less severe antagonist-precipitated withdrawal syndrome. Administration of naloxone was associated with the increased expression of TNF-α, GFAP, Iba1 and iNOS in the brain samples of morphine dependent mice, while the nine days treatment with both 5 and 10 mg/kg simvastatin reduced such changes.

Conclusion: The obtained results showed that the protective effects of simvastatin against both tolerance to nociceptive effects of morphine as well as withdrawal-induced behavioral profile are meaningful. Inhibition of glia

activity as well as antioxidant effects of pharmaceutical simvastatin further proves its neuroprotective property.

Keywords: Morphine tolerance, Morphine withdrawal, Simvastatin, Glia, Proinflammatory cytokines

Single-nucleotide polymorphism of rs11061971 (+219 A>T) in adiponectin receptor 2 (AdipoR2) gene and its association with risk of type 2 diabetes among an Iranian population (Research Paper)

Masoud Tahani,[1] Mohammad Taghi Goodarzi,[2,*] Ali Asghar Ahmadi,[3] shiva Rakhshaninasab,[4] Alireza Farrahi,[5] Akram Mehrzad Selakjani,[6]

1. Department of Biochemistry, Islamic Azad University, Shahrood Branch, Shahrood, Iran
2. Department of Biochemistry, Islamic Azad University, Shahrood Branch, Shahrood, Iran
3. Northern Research Center, Pasteur Institute of Iran, Amol, Iran
4. Department of Biochemistry, Islamic Azad University, Shahrood Branch, Shahrood, Iran
5. Department of Biochemistry, Islamic Azad University, Shahrood Branch, Shahrood, Iran
6. Department of Biochemistry, Islamic Azad University, Shahrood Branch, Shahrood, Iran

Introduction: Genetic modifications in the adiponectin receptor 2 (AdipoR2) gene can affect phenotypes associated with insulin resistance and diabetes. The purpose of this study was to evaluate the possible role of genetic modifications in the AdipoR2 gene, to determine the frequency of genotypes and polymorphism alleles of this gene at rs11061971 (+219 A>T), and to investigate its correlation with type 2 diabetes (T2D) and its related metabolic profile.

Methods: In this case-control study, the single-nucleotide polymorphism (SNP) of interest in 116 T2D patients and 102 controls was evaluated using RFLP PCR and FOK 1 enzyme. Fasting blood sugar, cholesterol, triglyceride, insulin, HDL-C, LDL-C and HbA1c were also measured and their correlation with the studied genetic modifications was assessed. The collected data were analyzed using Chi-square test and Hardy-Weinberg equation.

Results: There was a significant association in AT and TT genotypes in rs11061971 (+219 A>T) with T2D. However, no significant difference was observed in the frequency of alleles between the case and control groups. In addition, in LDL-C and total cholesterol in the control group, there was a significant difference between AA and TT genotypes as well as with AA and AT genotypes. However, no correlation was found between the other serum studied parameters and the genotype of individuals in the rs1106197171 polymorphism.

Conclusion: The role of rs11061971 (+219 A>T) polymorphism in T2D incidence seems to be strong. This study showed that AT and TT genotypes versus AA genotype increase the risk of diabetes.

Keywords: polymorphism, adiponectin receptor, diabetes, glucose, lipid

SMAD5/hsa-miR-28-5p/ FTX CeRNA axis affects colorectal cancer development by regulating " TGF-beta signaling pathway": bioinformatics gene expression profiling and RNA interaction analysis (Research Paper)

MahsaSadeghi,[1,*] Mohammad Rezaei,[2] Mansoureh Azadeh,[3]

1. Zist Fanavari Novin Biotechnology Institute, Isfahan, Iran
2. Zist Fanavari Novin Biotechnology Institute, Isfahan, Iran
3. Zist Fanavari Novin Biotechnology Institute, Isfahan, Iran

Introduction: Colorectal cancer (CRC) is one of the most common malignant diseases in the world, and its incidences increased with age. Colorectal cancer develops slowly but can spread to surrounding and distant tissues of the body. Approximately 95 percent of colorectal cancers involve the glandular cells in the wall of the colon and are called adenocarcinomas. Other colorectal cancers may begin among hormone-producing cells, immune cells, or underlying connective tissue. Competitive endogenous RNAs (ceRNAs) theory have revealed a new mechanism of interaction between RNAs (mRNAs, miRNAs and lncRNAs) that is used to find the involved genes. In this study we used microarrays to detail the global programe of gene expression underlying different lines and stages of patient-derived colorectal cancer organoids to target novel biomarkers for diagnosis and curing CRC.

Methods: First, GSE117548 were downloaded from NCBI Gene Expression Omnibus (GEO) and analyzed using limma package to identify differentially expressed genes (DEGs) in different stages which are screened by RStudio software. SMAD5, DUSP4, PHLDA1 and IGF2 with these conditions (|logFC| > 2 and adjusted p-value< 0.05) were taken to the miRWalk 2.0 database to select the miRNAs related to the gene, next in LncBase v.3 miRNAs were searched and several lncRNAs were found which is called FTX, APTR,DLEU1 and H19. The binding and paring scores of these microRNAs have been studied which the interaction of them have been showed as a Cystoscope software.

Results: In the end, after analysis of total RNA from 16 human patient-derived colorectal cancer organoids. we obtained 264 DEGs composed of 78 upregulated and 186 downregulated genes. This analysis outcomes assigned that the GSE117548 were surprisingly enriched in several biological mechanisms. The candidate hub genes were searched in Kyoto Encyclopedia of Genes and Genomes (KEGG) database to find the pathways which they are participated in separately. Upregulated gene pointed CRC-related pathways named, TGF-beta signaling pathway which is named SMAD5 that illustrates as a vital gene of these pathways.

Conclusion: we measured differential expression genes in stage 3 to stage 4 of this cancer to find the invasion of cells and prevent metastasis. Several lines of evidence suggest that SMAD5 and PHLDA1 have an important role in cancer. SMAD5 is a Transcriptional modulator activated by BMP (bone morphogenetic proteins) type 1 receptor kinase and also involved in Signaling pathways regulating pluripotency of stem cells. PHLDA1 is a potential transcriptional activator that acts as a modulator of apoptosis and cell proliferation so The results of this study indicate that there might be a CeRNA network between SMAD5, DUSP4, PHLDA1 and hsa-miR-28-5p.moreover, the presence of SMAD5 and PHLDA1 in this network , reinforces the possibility of PHLDA1 being a reliable biomarker for detect the metastasis of cancerous cells.

Keywords: Microarray, Colorectal cancer, PHLDA1, SMAD5, Bioinformatics, CeRNA, Systems biology,FTX

social health (Research Paper)

Amirhosein zand,[1,*]

1. Faculty of pharmaceutical sciences

Introduction: From a healthcare perspective, mass gatherings – such as music festivals and pilgrimages – present complex and multifaceted health risks that can strain healthcare systems (e.g., disease transmission, environmental stressors, and substance misuse; Memish et al., 2019; World Health Organization (WHO), 2015). Yet, as an emerging and rapidly evolving multidisciplinary field, mass gathering medicine remains theoretically underdeveloped (Memish et al., 2019; Steenkamp et al., 2016). Research and practice have tended to focus on physical factors in the aggravation and mitigation of risks in mass gatherings, while often ignoring psychosocial factors (Hopkins & Reicher, 2016a, 2016b, 2017). The WHO (2015) has recognised this paucity and highlighted the need for mass gathering management and research to "consider psychosocial elements in the planning and monitoring of events to ensure public safety" (p. 149). The present research provides a social-psychological perspective of the aggravation and mitigation of mass gathering-associated health risks by exploring perspectives of healthcare professionals (HCPs) operating in two mass gathering settings: a Catholic pilgrimage and music festivals.

Methods: Semi-structured interviews, complemented by a brief survey, were conducted with 17 HCPs in the United Kingdom operating at a religious pilgrimage and music festivals.

Results: The findings from a thematic analysis suggest that HCPs recognise that social identity processes involved in identity enactment in mass gatherings are implicated in health risks. HCPs also perceive value in drawing on social identity processes to inform and improve healthcare practices and interventions in mass gatherings. The findings from the survey corroborate the findings from the interviews.

Conclusion: Taken together, the research highlights avenues for future research and collaboration aimed at developing healthcare practices and interventions informed by the social identity approach for the management of health risks in mass gatherings.

Keywords: Social identity, Mass gatherings, Crowds

Social Media and Fertility Knowledge (Review)

Mina Soleimani,[1,*] Hanane Hamidi,[2] Fatemeh Mohebi,[3]

1. MSc in Midwifery, Iran University of Medical Sciences, Tehran, Iran
2. Undergraduate nursing student, Khalkhal University
3. Molecular Medicine Research Center Hormozgan Health Institute, Hormozgan University Of Medical Sciences, Bandar Abbas,

Introduction: Postponing in becoming parent has steadily increased during the past decades in some countries. Studies show that many social, economic and individual factors contribute to the lower fertility behavior among new generations. Apart from these, poor fertility knowledge and misconceptions might be responsible for delay in childbearing among young couples. On the other hand, the pervasiveness of media into our everyday lives, can be demonstrated by their ability to influence aspects of our cognitive function including attention, knowledge, and awareness. Therefore, there is a serious need for correct reproductive and fertility health knowledge before pregnancy for public through social media. The aim of the present study was to what extent interventions and information within social media can positively impact health behaviors.

Methods: In this review article we comprehensively studied more than 30 article of PubMed/MEDLINE, Web of science, and science direct from 2010 to 2021.

Results: 27 studies show that there is a significant relationship between educational fertility information and childbearing decision and about 3 studies didn't find anything significant. Unlike other high-cost interventions, this low-cost educational intervention had helped couples for making informed fertility decisions. There was slight difference in the effect of the type of provided educational packages including videos, lectures and smartphones app.

Conclusion: According to these studies we can conclude that social media can promote fertility knowledge and to reduce involuntary childlessness between young couples who postpone their first birth while they might not have any important social and economic obstacles. But, there was a lack of depth in this information and collaboration with counselors which this intervention can be solved with accurate and specialized design and follow-up by consultants.

Keywords: fertility knowledge, reproductive awareness, technological education

Spoilage of Chicken Meat With Salmonella spp Distributed in Yazd City, Iran (Research Paper)

Mohammad Javad Forouzani-Moghaddam,[1,*] Ruholla rahimi nasab,[2] mostafa rahimi nasab,[3]

1. Msc of Food Microbiology, School of Paramedical, Iran University of Medical Sciences, Tehran, Iran
2. Bachelor of Biotechnology, Yazd University, Yazd, Iran
3. Bachelor of Biotechnology, Yazd University, Yazd, Iran

Introduction: Foodborne diseases are one of the fundamental problems in the world. Salmonella is one of the most important foodborne bacteria, which is responsible for the prevalence of foodborne diseases in humans. The aim of this study was to investigate the presence of Salmonella in distributed chicken meat in Yazd city, Iran.

Methods: In this study, 125 samples of chicken meat were selected from Yazd city and investigated for the presence of Salmonella. Each sample was cultured in selenite cystine medium and incubated at 37°C for 24 hours. Then the obtained colonies were cultured in MacConkey agar and Salmonella-Shigella agar. Finally, biochemical and antibiogram tests were performed on isolated Salmonella samples.

Results: Totally, 9 chicken samples (7%) were found to be contaminated with Salmonella. All of the isolated Salmonella samples were identified as Salmonella enteritidis. All of S. enteritidis isolates (100%) showed the highest resistance to erythromycin and ampicillin antibiotics. All of the tested isolates (100%) showed sensitivity to gentamicin.

Conclusion: Our study showed high prevalence of Salmonella in distributed chicken meat in Yazd city. Therefore, the improvement of health conditions in food preparation centers is highly recommended.

Keywords: Spoilage, Chicken meat, Salmonella, Yazd

Statins and 5-fluorouracil Resistance: An Insight into Signaling Pathways (Review)

Elham Norouz Dolatabadi,[1] Vahid Asghariazar,[2] Maryam Darvish,[3,*] Kazem Nejati koshki,[4]

1. Biotechnology department, Arak university of medical sciences, Arak, Iran
2. Immunology research center, Ardabil university of medical sciences, Ardabil, Iran.
3. Biotechnology department, Arak university of medical sciences, Arak, Iran
4. Pharmaceutical Sciences Research Center, Ardabil University of Medical Sciences, Ardabil, Iran

Introduction: 5-Fluorouracil (5-FU) is part of a group of chemotherapy drugs that are widely used to treat cancer. 5-FU exerts its anticancer effects by inhibiting thymidylate synthase (TS) and incorporating its metabolites into RNA and DNA. Despite its anticancer effects, 5-FU monotherapy was reported by Johnston and Kaye to have low response rates in the range of 10%-20%. These limitations of 5-FU-based therapies are due to drug resistance. P53 protein as a tumor suppressor by inducing pro-apoptotic genes and decreasing anti-apoptotic genes leads to the onset of apoptosis and cell death. Although in vitro studies have shown that loss of p53 function decreases cell sensitivity to 5-FU by over-activating the Ras / PI-3K / PTEN / AKT / mTOR and Ras / Raf / MEK / ERK signaling pathways and finally increases 5-FU resistance. HMG-CoA inhibitors (statins), a class of drugs that reduce cholesterol, manage and prevent coronary heart disease. They are among the most commonly prescribed drugs worldwide. Statins are inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMG-CoA reductase), the rate-limiting enzyme in the mevalonate pathway. Mevalonate is involved in synthesizing isoprenyl proteins, dolichol, and ubiquinone that play several important roles in cellular functions. Mevalonate-derived prenyl groups, farnesyl pyrophosphate (FPP) and geranylgeranyl pyrophosphate (GGPP), facilitate essential intracellular functions of various proteins such as Ras. Disruption of these processes in neoplastic cells by statins leads to the control of tumor onset, growth, and metastasis, which prevents the growth of cancer cells and leads to cell death and apoptosis. Preclinical data suggest statins exhibit pleiotropic antineoplastic effects in various tumors, but clinical studies have provided conflicting data as to whether statins influence the risk of cancer. The previous study showed that the combination of statins with other drugs, such as low-dose aspirin or safer non-steroidal anti-inflammatory medications, may be useful in preventing and treating different cancer.

Methods: PubMed, Embase and Google scholar databases were searched for related articles.

Results: Overuse of 5-fluorouracil to treat cancer causes drug resistance. Therapeutic combination of fluorouracil with statins can reduce this drug resistance

Conclusion: Evidence suggests that the use of statins could reduce drug resistance to different cancer. So they may be a suitable method for combination cancer treatment. This group of drugs can reduce the resistance to 5-Fluorouracil by regulating signaling pathways such as Ras / PI-3K / PTEN / AKT / mTOR and Ras / Raf / MEK / ERK in a different type of cancer.

Keywords: Statin; Cancer; Signaling Pathways; Drug resistance; 5-Fluorouracil

Stem cells and bone regeneration: a review (Review)

Nafiseh baheiraei,[1,*] Nayereh Ahmadian,[2]

1. Tissue Engineering & Applied Cell Sciences Division, Department of Anatomical Sciences, Faculty of Medical science, Tarbiat Modares University, Tehran, Iran
2. Department of Bio-Computing, Faculty of Interdisciplinary Science and Technologies, Tarbiat Modares University, Tehran, Iran

Introduction: Bone defects that is caused by disease and traumas have become a clinical challenge which seriously affect the health and life quality especially amongst the elderly. Cell therapy which has gained an increasing attention toward itself lately, has offered new methods to treat incurable diseases. Stem cells are able to improve angiogenesis and prevent fibrosis that leads to heal the damaged tissue. Hence, they have an important role in tissue regeneration and repair. The objective of this work is to review the recent researches on stem cell therapy for bone regeneration; compared with other current treatments.

Methods: Electronic databases were searched.

Results: Implantation of cells in combination with scaffolds results in greater bone regeneration compared with transplantation of cells alone. Mesenchymal stem cells (MSCs) seem more acceptable to be used in clinical trials compare to other stem cells for bone repair.

Conclusion: Among various cells used for cell therapy, MSCs have therapeutic potential holding several advantages over conventional treatments in bone regeneration. However, more researches is needed to understand the mechanisms underlying their therapeutic efficacy which could direct clinical decision-making.

Keywords: Bone regeneration, Cell therapy, Mesenchymal stem cells, Scaffolds

stem cells and recreation (Review)

kianoosh ziaei,[1,*] Mohammad Taghi Mohseni,[2]

1. Dr. Hesabi High School
2. Dr. Hesabi High School

Introduction: In recent years, the prevalence of chronic diseases, such as cardiovascular diseases, diabetes, neurotransplantation, etc., has been reported Challenge for treatment has more effective. Considering the medical investigation that was carried out to rehabilitate and reduce the damage caused by diseases such as stroke, types of cancer, heart attack, pulmonary problems and so on. It has made significant progress with stem cells, which is very promising.

Methods: This paper describes basic concepts, application and limitation of appropriate usage and also an overview of stem cell immunization and decreasing it in clinical application of cells by collecting the data and previous researches.

Results: Considering the medical investigation that was carried out to rehabilitate and reduce the damage caused by diseases such as stroke, types of cancer, heart attack, pulmonary problems and so on. It has made significant progress with stem cells, which is very promising.

Conclusion: Stem cells exist in all the multi-cell organisms and the ability to divide and transform into very specific cells and also the ability to replace damaged or eliminated cells, the effects of stem cells in experiments, have increased the importance of research and research in this field. However, there are some obstacles in clinical application of stem cells which are the most important immunogen and subsequently immune response, so further researches are required to understand their biology. Nowadays, extensive research in stem cells technology is done to prevent the use of these cells to treat diseases, repair and reconstruct tissues, and build these cells. According to its variety: The embryonic cells, umbilical cord blood and adult cells are different in these experiments and there have been a number of solutions recently for reducing the duration of development of stem cells. Doctors have transplanted stem cells, which are also referred to as bone marrow transplants. In stem cell transplantation, stem cells are supplanted by chemotherapy or disease or they serve as a way for the donor's immune system to combat certain types of cancer and blood-related diseases such as leukemia, lymphoma, neurooblastoma and multiple myeloma. In these bonds, we use adult and umbilical cord blood stem cells. Also, the complications of CVA are reduced significantly and correlated with patients suffering from heart

disease and awaiting transplantation, along with prescribing the immunosuppressive drugs, the cord blood transplantation method is used as an aid method. Constipation of stem cells has achieved good results in other patients. In the past year, due to the emergence and proliferation of the Coid Virus (CADV), the researchers have succeeded in transforming the stem cells into lung cells. The first step has been taken to further studies quickly due to the emergence and proliferation of the C19 virus, because the patients with severe lung problems are increasing rapidly.

Keywords: Stem cells, bone marrow, franchise stem cells, immunogenicity, clinical application

Stem cells as a carrier of the therapeutic agent in the gene therapy of glioblastoma (Review)

Yasamin Ghaffari,[1,*]

1. Tarbiat Modares University

Introduction: Glioblastoma is the most common, invasive, and deadliest of all primary brain tumors and accounts for 45.2% of malignant tumors of the central nervous system. Poor prognosis reduces the likelihood of these patients recovering and increases their risk of death. The one-year survival rate of these patients is reported to be 35%. The first step in treating patients with glioblastoma is the surgical removal of the tumor. Use of temozolomide chemotherapy in addition to common treatments such as surgery and resection. Tumor and radiation therapy have increased patients' life expectancy, but only 5% of patients survive after initial diagnosis. One of the reasons for the low success of common treatments for this tumor is the inherent resistance of the tumor to chemotherapy and radiotherapy. Also, complete surgery of the tumor is not possible due to the special position and aggressive nature of the tumor, the presence of the blood-brain barrier, cancer stem cells, and tumor heterogeneity are other reasons for the difficult treatment of this disease. Therefore, new therapeutic strategies to target and kill glioblastoma cells need to greatly increase the effectiveness of treatment. One of the targeted therapies for this disease is gene therapy, which to some extent overcomes the mentioned therapeutic challenges, especially low tumor blood flow, and blood-brain barrier. There are currently four types of potential gene therapy in GBMI therapy: Suicide genes, which cause the local production of toxic compounds; Immune-mediating genes, which enhance or enhance the anti-tumor immune response; Tumor suppressor genes, which induce apoptosis in cancer cells; and treatment with oncolytic viruses, which lysis tumor cells and deliver a variety of therapeutic genes. It is now important to design safe vectors with long-term gene expression, as well as to develop a highly specific method for identifying gene therapy target cells and regulating the expression of those genes by micromolecules. Delivery systems include direct gene delivery (viral and non-viral vectors such as liposomes, micelles, and nanoparticles), tumor-oriented cell carriers, and intelligent carriers. One of the carriers of gene therapy is stem cells, which we will discuss in this article. The most important limitation of the presentation of genes by viral vectors is that they are not able to infect all cancer cells, but stem cells do not. Neuronal stem cells, mesenchymal stem cells, and induced pluripotent cells are three suitable candidates for vector gene therapy.

Methods: Publications were retrieved by a systemic search of multiple bibliographic databases, including Medline, Embase, Scopus, Biomed central,

PubMed and google scholar. The search was narrowed to the original articles published in English from2019 to 2021.

Results: Neuronal stem cells have a natural tendency towards brain tumor tissue. The tumorigenic capabilities of NSCs and their ability to stably express the presented genes make them ideal cell carriers. Another interesting aspect of NSCs is that they can be delivered to the skull not only through systemic injections but also through an intranasal route. Empirically, NSCs contain a variety of genes and are successfully delivered to the tumor site. For example, in combination with oncolytic adenoviruses in the in vivo test, they effectively target the tumor and reduce tumor growth. NSCs are also designed to transport cytokines, nanoparticles, and enzymes to convert ineffective prodrugs to chemotherapeutic drugs. Mesenchymal stem cells are relatively easy to separate from NSCs and can be obtained autologous from the bone marrow and manipulated back into the same patient. As a result, they prevent an allogeneic response in the carrier. MSCs are also designed to express TRAIL and CD with strong antitumor effects. Another type of cellular carrier is iPSCs. The benefits of using iPSCs instead of stem cells include their ability to escape rejection by the immune system and the absence of ethical concerns when using human embryonic cells. In addition, iPSCs can be easily manufactured from somatic cells, making them an ideal choice for research on many model systems.

Conclusion: The ineffectiveness of common therapies in the most invasive brain tumors opens a new window for targeted therapies. The effectiveness of current glioblastoma treatments can be enhanced by more effective and designed methods. New smart carrier design strategies in combination with conventional therapies, will be a hope for increasing the survival of these patients.

Keywords: Glioblastoma, Stem cells, Gene therapy, Drug delivery, Drug carriers

Stress and cancer (Review)

hasti saadati,[1,*]

1.

Introduction: Nowadays cancer is one of the most important health issues and it is one of most common causes of death throughout the world. 1 in 8 people gets cancer daily. In modern societies, chronic stress has been involved in the pathogenesis of many diseases, consisting of cancer. This article aims to indicate the relationship between stress and cancer based on recent studies.

Methods: This article is a review study by searching databases such as Google Scholar, PubMed and SID using the keywords stress and cancer is done. As a result of the search, 7 articles were selected for review after studying.

Results: Most of studies demonstrate significant association between phycological stress and the onset and recurrence of cancer. Studies have revealed stress weakens the immune system and put body at risk of developing cancer cells. Chronic stress triggers the activation of specific signaling pathways in cancer cells and the tumor microenvironment, resulting in tumor growth and progression. it is reported that occurrence of oxidative stress due to increased active species and decreased efficiency of antioxidant defense system, stimulates angiogenesis and metastasis in cancer cells, which are major factors of spread and development of cancer.

Conclusion: Stress can results in occurrence of cancer and can accelerate cancer development and aggravate disease side-effects.

Keywords: Stress-cancer

Structure-based drug design of proteins as a novel therapeutic perspectives (Review)

Armin Mokhtariye,[1] Mohammad Reza Mofid,[2,*]

1. Department of Clinical Biochemistry, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran
2. Department of Clinical Biochemistry, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

Introduction: Structure-based drug design (SBDD) of protein ligands has emerged as a new tool in medicinal chemistry. The goal of SBDD is to identify a suitable compound for clinical testing (drug candidate) by designing and optimizing of a chemical structure. It is based on knowledge of the drug's three-dimensional structure and how its shape and charge cause it to interact with its biological target, ultimately eliciting a medical effect. There are numerous drugs available on the market that have been identified by SBDD, as a successful experience; Human immunodeficiency virus (HIV)-1 -inhibiting FDA-approved drugs.

Methods: SBDD proceeds through multiple cycles leading an optimized drug candidate to clinical trials. In the first phase, a potential therapeutic target and active ligands are identified. The fundamental step involves cloning of the target gene followed by the extraction, purification, and 3D structure determination of the protein. A complete investigation of the electrostatic properties of the binding site can be performed using a 3D structure of the target molecule. These molecules are ranked according to a scoring system based on electrostatic and steric interactions with the binding site. In the second phase, the top hits are synthesized and optimized. The next step is to determine the 3D structure of the target protein in complex with the promising ligand obtained in the first phase. The third phase includes clinical trials of the lead compounds.

Results: Those compounds that pass the clinical trials proceed to the fourth phase in which the drug is distributed in the market for clinical use.

Conclusion: In conclusion, bioinformatics offers several approaches for the prediction of structure and function of proteins on the basis of sequence and structural similarities. SBDD has made significant improvements in the structural properties of biomolecules and the rational drug design. Some drugs are as a successful experience that have been identified by SBDD; Human immunodeficiency virus (HIV)-1 -inhibiting drugs. However, despite a

lot of improvements and currents developments in SBDD, a consistent solution is yet to be developed.

Keywords: Structure-based drug design, 3D structure, Bioinformatics, molecular biology

Study of PHOX2B , ELP1, and MAP2 genes expression in bone marrow-derived mesenchymal stem cells after treatment by glabridin for differentiation into nerve-like cell (Research Paper)

Maryam Hamidi,[1] Hossein Fahimi,[2] Hora Jalali Tehrani,[3,*]

1. Department of Developmental Biology, Faculty of Advanced Science and Technology, Tehran Medical sciences , Islamic Azad university ,Tehran, Iran
2. Department of Genetics, Faculty of Advanced Science and Technology, Tehran Medical sciences , Islamic Azad university ,Tehran, Iran
3. Department of Developmental Biology, Faculty of Advanced Science and Technology, Tehran Medical sciences , Islamic Azad university ,Tehran, Iran

Introduction: Mesenchymal stem cells can differentiate into all types of cells. Mesenchymal stem cells derived from bone marrow can differentiate into neuron- like cells in vitro conditions. Important genes in this process are ELP1, PHOX2B and MAP2. Glabridin is a polyphenolic flavonoid derived from the roots of licorice. Use of glabridin on cell differentiation was studied.

Methods: Mesenchymal stem cells derived from bone marrow was incubated. Toxication levels of glabridin was determined by MTT Assey test in concentrations of 5, 10, 20, 40 and 80 µM. CDNA was synthesized and the amount of change in gene expression was studied by real time PCR.

Results: Glabridin fatality dosage was tested by MTT in 40 and 80 µM concentration and based on 24 hour analysis, ELP1, PHOX2B and MAP2 gene expression in samples incubated with glabridin had significant increase compared to the control group.

Conclusion: Results from the study showed that glabridin of mesenchymal stem cells derived from bone marrow cause increased ELP1, PHOX2B and MAP2 gene expression resulting in increase in their differentiation into neuron- like cells. So glabridin can be used for increased differentiation into neuron- like cells.

Keywords: Mesenchymal stem cells, Neuron- like cell, Glabridin

Study of association between codon31 of p21 (rs 1801270) gene single nucleotide polymorphisms (SNP) with the risk of colorectal cancer in khuzestan province (Research Paper)

Mina Dabirzadeh,[1] Mohammad Mohammadi,[2,*]

1. Shahid Chamran University
2. Shahid Chamran University

Introduction: Cancer is in most cases one of the most deadly diseases that causes many problems to the patient in terms of quality of life and imposes huge economic costs on the patient's family and society. Cancer occurs as a result of uncontrolled proliferation of cells and is the second leading cause of death in the world, and one of the most deadly types of cancer is colon cancer. One of the most important proteins involved in fighting cell cancer is the p21 protein, and a defect in the activity of this protein can cause changes in its structure and activity.

Methods: In this study, this polymorphism was studied among the population with colorectal cancer in Khuzestan province by RFLP method. For this purpose, 112 patients with colorectal cancer and 100 control samples of polymorphism were studied. After sampling, osmotic shock or ionic detergents were used to extract the cell extract. The DNA-bound proteins were then digested and the cellular proteins were precipitated by phenol and chloroform or saturated NaCl (6 M), and finally, the DNA was precipitated with cold ethanol. To evaluate the quantity and quality of DNA, electrophoresis methods on agarose gel and nanodrop spectrophotometry were used. In this experiment, the polymorphism of the P21 gene was studied and part of the sequence of this gene was PCR, which contained the desired nucleotide, and after sectioning, the band difference was detected by the restriction enzyme. After performing RFLP and observing the pattern of different bands, sequences related to different patterns were sequenced and the results were compared with the natural gene sequence available at the NCBI site and the relevant genotype was determined. The experimental results were analyzed using SPSS software, version 21.

Results: PCR results of P21 gene showed that this gene contains a sequence with 221 nucleotides and the BIPI restriction enzyme cleaves the sequence when the target nucleotide is G; Therefore, the presence of a 221 nucleotide band on the gel electrophoresis indicates the cytosine amino acid codon, and the presence of 98 and 123 bp bands on the gel electrophoresis indicates arginine in the 21 codon of the P21 gene. Also, seeing three bands 221, 98 and 123 pairs of games indicates that the sample is heterozygous in this case. The amount of chi-square (chi-square) obtained by comparing the frequencies of the two groups in the three types of p21 gene genotype is

equal to 3.855. Given that the level of significance (p-value) is greater than 0.05; Therefore, there is no statistically significant difference between genotype in control group and patient in terms of p21 gene genotype.

Conclusion: Polymorphism in codon 31 (rs 1801270) is the most studied of the polymorphisms in this gene. During this polymorphism, C is displaced by A in the third codon of the p21 gene 31, and serine is unequivocally converted to arginine in a DNA-binding zinc finger motif. In this study, no significant difference was observed between patients with colorectal cancer and the control group in c21 polymorphism of p21 gene and codon 31 polymorphism of p21 gene did not show any effect on colorectal cancer in Khuzestan province.

Keywords: Colorectal Cancer, Polymorphism, p21, rs1801270, khuzestan

Study of association between codon72 of p53 (rs1042522) gene single nucleotide polymorphisms(SNP) with the risk of colorectal cancer in khuzestan province (Research Paper)

Mina Dabirzadeh,[1] Mohammad Mohammadi,[2,*]

1. Shahid Chamran University
2. Shahid Chamran University

Introduction: Cancer is caused by uncontrolled proliferation of cells and it is the second leading cause of death in the world and the third leading cause of death in Iran. Colorectal cancer is the growth of cancer cells in the colon or rectum and it is the second most common cancer among men after lung and prostate cancer and the third most common cancer among women after lung and breast cancer. The p53 protein is a transcription factor that is inactive in half of cancers and activated by DNA damage and induces transcription of genes involved in cell cycle control and apoptosis, and Codon 72 polymorphism of this gene can cause changes in its structure and activity.

Methods: This polymorphism was studied among the population with colorectal cancer in Khuzestan province by RFLP method and 112 patients with colorectal cancer and 100 control samples of this polymorphism were studied. Sampling was performed in containers containing EDTA and osmotic shock was used to extract the cell extract; and DNA-bound proteins were then digested by ionic detergents. The cellular proteins were then precipitated with phenol and chloroform or saturated NaCl solution, and finally, DNA precipitation was performed with cold ethanol. To evaluate the quantity and quality of DNA, electrophoresis methods on agarose gel and nanodrop spectrophotometry were used. In this experiment, the polymorphism of the P53 gene was studied and part of the sequence of this gene was PCR, which contained the desired nucleotide, and after sectioning, the band difference was detected by the restriction enzyme. After performing RFLP and observing the pattern of different bands, sequences related to different patterns were sequenced and the results were compared with the natural gene sequences available at the NCBI site and the relevant genotype was determined. The test results were analyzed using SPSS statistical software, version 21.

Results: The P53 gene PCR product is a sequence of 199 nucleotides, and the restricted enzyme BstUI cleaves the sequence when the target nucleotide is G; Therefore, the presence of a 199 nucleotide band on the gel electrophoresis indicates the proline amino acid codon, and the presence of two nuclei 113 and 86 nucleotides on the gel electrophoresis indicates arginine in the codon 72 of the P53 gene; Also, seeing three nucleotide bands 199, 86 and 113 indicates that the sample is heterozygous in this case. In the control group, 41% of the respondents have arginine / arginine genotype, 46%

have arginine / proline genotype and 13% have proline / proline genotype; While in the patient group, 32.1% of the respondents have arginine / arginine genotype, 43.8% have arginine / proline genotype and 24.1% have proline / proline genotype. The amount of chi-square (chi-square) obtained by comparing the frequencies of the two groups in the three types of p53 gene genotype is equal to 4.655 and there is no statistically significant difference between the genotype in the control group and the patient in terms of p53 gene genotype. The proline / proline genotype increases the chance of developing colorectal cancer by 2.365 times and is also statistically significant, given that the p-value level is less than 0.05.

Conclusion: Mutation in P53 is one of the most abundant single nucleotide genetic changes in human cancers. During polymorphism, codon 72 of exon 4 of the P53 gene, nucleotide C is converted to G, resulting in the conversion of proline CCC to arginine CGC, altering the original structure of P53. Although both structures function normally in binding activities to specific DNA sequences, they do show some functional differences. The arginine P53 allele shows greater apoptotic potency than the proline allele, and extensive research has been conducted on this polymorphism and cancer. Therefore, in this study, the effect of converting codon 72 of p53 gene to amino acid arginine in colorectal cancer was not observed in Khuzestan province.

Keywords: Colorectal cancer, polymorphism, p53, rs1042522, khuzestan

Study of The effect of human Wharton's jelly mesenchymal stem cells extract on collagen situation in skin wound healing process in rats (Research Paper)

Abdollah Abdollahpour,[1,*] Seyyed Esmael Safavi Khalkhali,[2] Bahram Amoghli Tabrizi,[3]

1. Department of Pathobiology, Faculty of Veterinary Medicine, Tabriz Branch, Islamic Azad University, Tabriz, Iran
2. Department of Pathobiology, Faculty of Veterinary Medicine, Tabriz Branch, Islamic Azad University, Tabriz, Iran
3. Department of Clinical Sciences , Faculty of Veterinary Medicine, Tabriz Branch, Islamic Azad University, Tabriz, Iran

Introduction: A wound is a disorder in natural structure, purpose and its interior soft layer of skin. To maintain the integrity of skin is vital to prevent bleeding, inadequacy of water, and entrance of microorganisms. Skin lacerations are occurred in accordance of different cases such as physical, chemical and biological damages. The point of healing jagged part on our skin has been under the studying of scholars and researchers with minimum of side effect. Hence different ways and protocols have been proposed and tried with it. One of the most important factors in wound healing is the collagen situation. New fibroblasts begin to produce collagen very quickly, and this can be detected in wounds very early on the second day of injury. Collagen synthesis continues for some time after injury. Collagen production is an important part of wound healing process before and after the formation of new tissue. There has been new methods of treatment originates from stem cells which aimed to rebuild and heal some tissues which these cells shown their efficacy in healing animal disease too. Stem cells with their Prodigious capabilities of propagation and rehabilitation are unique in other kind of cells. Such an evident source of stem cells is the blood of Umbilical cord. The use of the cells in blood faced with some limits. Therefore the examined researches in this field are trying to use the product of the cells such as cells extraction. The current survey is aimed with the efficacy of Mysenchymal stem cells of Wharton jelly Umbilical cord to treat a mouse wound.

Methods: This experiment conducted in two levels of invitro and inviro. The first invitro step was to separate and seed stem cells of Wharton jelly Umbilical cord. After the last time of doing this and centrifuge we got solutions of Wharton jelly Umbilical cord. In invivo stage with 30 vistar mouse which were grouped in a pair of 5 groups with the first group (normal) second group (control) was jagged as 3 groups included extract of 5, 10, and 20% division used. This injection was performed interior tissue in 1 Cc around the wound with physiology serum group and with examination gp was cell extract. Jagged laceration was created by surgical punch after anaesthesia and

epilation. After 21 days the death of mice some tissue models were gathered. The process of colouring by Van gison was conducted and histopolytical studies were taken into account. Also, some tissue models were gathered and proteins derived from the gene (Col-1α1) were examined by Western blotting.

Results: The results of this study showed In addition to faster healing of skin wounds in the treatment group, that the total intensity of collagen in all groups treated with cell extract was higher than the control group. The total intensity of collagen in the groups treated with cell extract was 10 and 20% significantly different from the control group. While the cell extract treatment group did not have a significant difference of 5% with the control group. It should be noted that the total intensity of collagen in the control group was significantly different from the healthy group ($P < 0.05$). It should be noted that the highest total collagen intensity in the treatment groups is related to 20%.

Conclusion: More and more collagen synthesis promotes the healing of skin wounds. Therefore, increasing collagen in the cell extract treatment groups causes faster healing of skin wounds.

Keywords: cellular extract, Mesenchymal stem cell, Wharton's jelly, Skin wound, Collagen

Studying the effect of serial passages in human mesenchymal stem cells on gene expression of TERT and miR-138 genes in vitro (Research Paper)

Sami Beit Sayah Ozari,[1] Seyedeh Fatemeh Azghadi,[2] Amir Atashi,[3,*]

1. Department of Hematology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran
2. Student Research Committee, School of Allied Medical Sciences, Shahroud University of Medical Sciences, Shahroud, Iran
3. Department of Hematology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran

Introduction: Mesenchymal stem cells (MSCs) are of great significance in tissue engineering and disease treatment. There is a small number of these cells in the body. Therefore, their expansion is needed for clinical applications. However, in vitro expansion can shorten telomere length, cause aging in cells, and decrease their quality in cellular therapy. In this study, the goal is to assess the expression of miR-138 gene as a known telomerase regulator through consecutive MSCs passages.

Methods: MSCs isolation was conducted by RosetteSep kit from human bone marrow aspiration. After five passages, mRNA and miRNA were isolated via TRIZOL through the phenol-chloroform method. cDNA was synthesized, and the expression of miR-138 gene and TERT were evaluated through Real-Time PCR.

Results: The outcomes indicated a significant decrease in the expression of TERT gene after one passage. A notable increase in miR-138 expression was detected as well ($p<0,05$).

Conclusion: Evaluating the expression of miR-138 and TERT genes in expanding MSCs indicates the potential use of miR-138 in increasing the capability of in vitro MSCs expansion.

Keywords: Mesenchymal Stem Cells, Telomerase, Expansion, miR-138

Successful production of soluble and active single domain antibody against human IL-1RAP (Research Paper)

Aref Farokhi-Fard,[1] Fatemeh Davami,[2,*]

1. Biotechnology research center, Pasteur institute of Iran, Tehran, Iran
2. Biotechnology research center, Pasteur institute of Iran, Tehran, Iran

Introduction: Acute myeloid leukemia (AML) is the most prevalent leukemia in adults with the lowest survival rate. Targeted therapy could be a valuable strategy against AML. Antibodies are of most examined targeting agents. Interleukin 1 receptor accessory protein (IL-1RAP) is an excellent biomarker for targeted therapy of myeloid leukemia. Although the presence of partner domain is necessary for human and murine VH domain to be stabilized, single domain antibodies (sdAbs) as the tiniest antigen binding immunoglobulins could be designed by engineering of VH domain. The production of active and stable VH domain in sufficient quantity is practically problematic due to folding difficulty and aggregation propensity of un-engineered VH. So the reports are extremely rare in this area. Here, we report the bacterial production of a stable un-engineered VH domain against human IL-1RAP. This study may be beneficial for further analyses of single domain antibody properties.

Methods: The coding sequence of anti-IL-1RAP scFv were extracted from a patent (PCTIUS20131077323: SEQ ID NO 13 for VH and SEQ ID NO 14 for VL) which is about a murine antibody developed against 12 residues peptide that is exclusively present in membrane anchored isoform of human IL-1RAP. The scFv coding DNA fragment (VH-(G4S)5-VL arrangement) was artificially synthetized and sub-cloned in pET32a expression vector at NcoI and XhoI sites. Colonies were screened by colony PCR using T7 universal primers. Plasmid extracted from PCR+ clone (C13) was confirmed by PCR and enzymatic digestion. C13 plasmid was then transformed to T7 promoter-based expression host, Origami B strain and the transformants were selected on LB agar plate containing kanamycin, tetracycline and ampicillin. A single colony of Origami B/C13 was cultured in Luria-Bertani (LB) broth medium with the same antibiotics, induced (0.05 mM IPTG, 30 °C, 200 rpm for overnight) and subjected to purification by Ni-NTA affinity resin (Qiagen) in native condition. The eluted protein was concentrated and buffer exchanged to 50 mM Tris-HCL pH 8 by use of centrifugal amicon filter (10 KDa cut off). Protein quantification was accomplished by NanoDrop (Abs280nm, at extinction coefficient of 43,890 M-1 cm-1). Binding activity was evaluated by cell based enzyme-linked immunosorbent assay (ELISA) duplicately on K-562 cells fixed by formaldehyde with different concentrations of Trx-VH and using polyclonal anti-His-tag antibody.

Results: The recombinant protein was successfully purified by NiNTA. The productivity (calculated after concentration and buffer exchange) was estimated to be round 5 mg/L LB culture. The eluted protein exhibited an apparent molecular weight (MW) of ~ 30 kDa (15 kDa lighter than the expected MW). So, we speculated that the lost fragment was pertaining to VL, because the scFv had no C-terminal his-tag and could only be purified through the His-tag located on the upstream of VH. Analysis of insoluble pellet of the centrifuged lysate by SDS PAGE showed a very intense band of 45 kDa. So, we came to the conclusion that the truncation is due to severe proteolysis which removed the VL domain. Binding assessment of purified protein showed that produced VH domain was active, however, as expected, the affinity was relatively low (OD450nm values of 0.05, 0.185 and 0.205 at concentrations of 25, 50 and 100 µg/ml of Trx-VH respectively).

Conclusion: We fortuitously get substantial quantities of soluble active VH domain from a scFv coding construct. We guessed that the proteolysis may be related to the Trx, because, we previously expressed and purified this scFv construct (without Trx) in soluble form in cytoplasm of SHuffle strain. This assumption, however need more researches. Despite the general agreement on instability of un-engineered VH domain, the VH domain we produced was completely stable even after concentrating to 3 mg/ml. This could be explained by in vitro solubility enhancement effect of Trx-tag. We believed that overall avidity derived from several VH in targeted drug delivery vehicles could trivialize the low affinity of single VH domain. More investigations are needed for detailed insight into structural properties and binding kinetics of the described antibody fragment.

Keywords: AML, single domain antibody, scFv, IL-1RAP

Supporting Self-Management in Children with Covid-19 Disease: A Narrative Review (Review)

Seyed Mohsen Laal Mousavi,[1,*] Homa HajiZadegan,[2] Zeinab Habibi,[3] Pegah Farzanegan,[4] Maedeh Fakhrodini,[5]

1. Department of Health Information Technology, Faculty of Paramedical, Mashhad University of Medical Sciences, Mashhad, Iran
2. Department of Health Information Technology, Faculty of Paramedical, Mashhad University of Medical Sciences, Mashhad, Iran
3. Department of Health Informatics, Faculty of Medical Science, Tarbiat_Modares University, Tehran, Iran
4. Department of Dentistry, Faculty of Medical Sciences, Babol University of Medical Sciences, Babol, Iran
5. Department of Midwifery, Faculty of Medical Sciences, Islamic Azad University, Ardabil Branch, Ardabil, Iran

Introduction: COVID-19 is a contagious disease. The covid-19 pandemic can affect both adults and children. Children are as susceptible as adults in indicating. Self-management support includes the cooperation of the patient, family, and health care providers. The quarantine events of the covid-19 pandemic changed children's routine, so we need more efficient childcare instructions than before.

Methods: We searched articles in public record databases on the Internet like Google Scholar database and SID, Science Direct, PubMed, Up-to-date using the MeSH, keywords including Self-Management, Children, Covid-19 and related factors, articles, and guidelines related to the subject of the paper from 2019 to 2021.

Results: Self-management in children is an emerging issue. There are three challenges: 1) children's dependence, 2) a wide range of growth factors affected by chronic disease, and 3) different epidemiology among children than adults. To achieve the more efficient method for self-management in children, we need a multidimensional model that has to include the following components: • Environment: Considering and recognizing all aspects of the child's environment - from family to community, • Body function: The physiology of Individual children should be examined and have their particular program • Activities: The standard amount of activity to be done and what can be done

Conclusion: This is an essential finding in understanding the self-management intervention in children with Covid -19. Self-management improves health outcomes by increasing the patient's ability to navigate

difficulties and solve issues, as well as boosting adherence to the treatment plan. As a final point, we need a multidimensional model that includes components to develop a more efficient technique for self-management in children. This result highlights that self-management interventions related to Covid- 19 conditions have many challenges and opportunities for children. In the future, hope for self-management intervention enhances chronic disease outcomes, especially the covid-19 condition in the children population. There must be no doubt that the development of self-management support techniques and technologies in the children population has been directed by evidence, increasing acceptance of best practices in health outcomes.

Keywords: Self-Management, Children, Covid-19

Switching Calcineurin Inhibitors Medication in Renal Transplant Recipients to Belatacept Therapy: A systematic review. (Review)

Mohammad Amin Talebpour,[1,*] Minoo Momenzadeh,[2] Amir Hussein Bueik,[3]

1. Student Research Committee, Islamic Azad University, Mashhad branch, Mashhad, Iran.
2. School of Medicine , Mashhad Islamic Azad University, Mashhad , Iran
3. School of Medicine , Mashhad Islamic Azad University, Mashhad , Iran

Introduction: Background: Conversion to belatacept immunosuppression is a therapeutic option for renal-transplant recipients with calcineurin inhibitors (CNI) toxicity, but it associates with a high risk of acute rejection. Gradual conversion and serial immune monitoring with urinary chemokine CXCL9 may allow increasing the safety of this maneuver.

Methods: Methods & Search strategy: The Cochrane Library, PubMed/MEDLINE, EBSCO (Academic Search Ultimate), ProQuest (Central), and Excerpta Medical databases and Google Scholar were searched using the keywords (CNI AND Nephrotoxicity prevention) OR (“Calcineurin inhibitor” AND Nephrotoxicity) OR (Tacrolimus AND Nephrotoxicity) OR (Ciclosporin AND Nephrotoxicity) OR (cyclosporine AND Nephrotoxicity) OR (Belatacept) OR (CNI Conversion) for the period from 1990 to 2020. Fifty-five related articles and reviews were found. Finally, out of the total number of studies, 21 full texts were available, and using JBI's Checklist for Randomized Clinical trials Studies and JBI's Checklist for Cohort Studies, 17 studies passed the quality evaluation stage and entered the study. The statistical population in all studies monitored renal function, metabolic profile, and circulating lymphocyte subsets. Three also quantified urinary CXCL9 over a 12-month follow-up period.

Results: Result: Seventeen studies including 875 renal transplant recipients (346 belatacept converted) were analyzed in our study. All of the patients in the belatacept group were successfully switched to belatacept immunosuppression at 3.3 (1.3-7.2) years after transplant. Nineteen patients had a reversible rise in serum creatinine, associated with acute rejection in 6 cases. Urinary CXCL9 increased before serum creatinine. After conversion, blood pressure and HbA1c significantly declined while eGFR and proteinuria remained stable. The percentage of circulating effector T cells and memory B cells significantly declined.

Conclusion: Conclusion: A better understanding of the mechanisms underlying calcineurin inhibitor nephrotoxicity could help in the individualization of therapy for and prevention of CNI nephrotoxicity.

Identification of high-risk patients for CNI nephrotoxicity before renal transplantation enables better use and selection of immunosuppression with reduced adverse effects and, eventually, successful treatment of the kidney recipients. Belatacept conversion is a good and safe option in patients with deteriorating renal function attributed to CNI nephrotoxicity.

Keywords: Keywords: Belatacepts, Calcineurin Inhibitors, Conversion, Nephrotoxicity, Renal transplant.

Sympathetic Role Over Metabolic Syndrome Activity (Review)

Mehrdad Ostadpoor,[1,*] Seyyed Hossein Heidari,[2] Pooria Rezaei,[3] Ahmad Zeinodini,[4]

1. Graduatedof Veterinary Medicine Faculty, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran
2. Graduatedof Veterinary Medicine Faculty, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran
3. Graduatedof Veterinary Medicine Faculty, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran
4. Graduatedof Veterinary Medicine Faculty, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran

Introduction: The metabolic syndrome (MetS) also called insulin resistance syndrome was originally described in 1988. it refers to the commonly occurring disorder comprising central obesity, systemic hypertension, insulin resistance and atherogenic dyslipidemia. it is associated with accelerated atherosclerosis in response to chronic inflammation, vascular endothelial dysfunction and presents significantly increased cardiovascular risk. Scientists have outlined diagnostic criteria for metabolic syndrome, which designates values for obesity (waist circumference or BMI), triglyceride levels, HDL levels, hypertension, hyperglycemia and sometimes urine albumin or albumin : creatinine ratio. among the components of metabolic syndrome, the quantity of insulin resistance and abdominal obesity have increased during the last decade.

Methods: In the current study, key words including Sympathetic, Metabolic Syndrome and Risk Factor 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 data was organized.

Results: Result shows increasing sympathetic nerve activity is vital in the dissipation of energy following food consumption through activation of beta-receptors. it is proposed that chronic sympathetic nerve activity can potentiate gaining weight and leading to obesity as a consequence of diminished sensitivity of beta-adrenoceptors. also in vitro and vivo studies clearly show that prolonged adrenergic stimulation results in desensitization of beta-receptor mediated responses. down regulation of beta-adrenoceptors leading to a blunted thermogenic response to food can potentiate insulin resistance and perpetuate the negative feedback cycle between insulin governing sympathetic outflows. in support of a primary role of the sympathetic nervous system in metabolic abnormalities that cluster to form the MetS, several prospective studies clearly show that increasing noradrenaline levels can precede clinical symptoms of obesity and hypertension. another study shows

the activation of sympathetic nerves in target organs like liver, pancreas, skeletal muscle, and adipose tissue can elicit acute catabolic responses. over activation of sympathetic nervous system is strongly associated with obesity and hypertension. in fact, enhanced Sympathetic nervous system activation exerts unfavorable effects like cardiac hypertrophy, arterial remodeling, and endothelial dysfunction on the cardiovascular system.

Conclusion: The sympathetic nervous system plays a pivotal role in regulating metabolic control. while acute sympathetic activation may be desirable under specific circumstances, it is clear that chronic stimulation of the sympathetic nervous system has the potential to augment risk for the MetS through the development of obesity, hyperglycaemia, insulin resistance, and hypertension.

Keywords: Sympathetic, Metabolic Syndrome, Risk Factor

Synthesis and characterization of bilayer biocompatible MOF-Chitosan nanoparticles conjugated with novel antiobiotic recombinant chimeric protein (Research Paper)

Mahnaz Malekian,[1] Sepideh Khaleghi,[2] Hossein Fahimi,[3,*]

1. Department of Biotechnology, Faculty of Advanced Science and Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.
2. Department of Biotechnology, Faculty of Advanced Science and Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.
3. Department of Genetics, Faculty of Advanced Science and Technology, Tehran Medical Science, Islamic Azad University, Tehran, Iran.

Introduction: Today overuse of antibiotics in the treatment of human and animal's diseases has caused multi drug resistance of bacteria against antibiotics. In addition, by using a handful of antibiotics, the resistance genes transmitted horizontally or vertically among a population. The enzymes purified from bacteriophages can play a role as an antibiotic. The aim of the present study was, to evaluate the function of chimeric endolysin antibiotic protein conjugated on the surface of MOF-Chitosan nanoparticles on gram-positive and gram-negative pathogenic bacteria.

Methods: Expression of chimeric endolysin protein in pET22, which was transformed in the BL21 host, was evaluated in TB and 2XYT media to optimize protein expression by 1 mM IPTG at 37 °C. Purification of chimeric endolysin protein was performed by NI-NTA affinity chromatography. Expression rate was assessed by SDS-PAGE. synthesis of MOF nanoparticles from, zinc acetate, bdc and dabco in dimethylformamide solvent were used. Then MOF nanoparticles were coated with, low molecular weight and the chimeric endolysin protein was conjugated to chitosan amine groups covalently (MOF-CS-CHAP(C)) and non-covalently (MOF-CS-CHAP(NC)). Finally, the physicochemical properties and morphology of nanoparticles were investigated by DLS, FTIR and TEM assays. Finally, to evaluate the antibacterial effect of nano particles against Pseudomonas aeruginosa, methicillin-resistant Staphylococcus aurous and Escherichia coli by MIC / MBC assay, the biofilm formation and synergistic with vancomycin were evaluated.

Results: Protein expression with TB medium in 18 hours by adding 5% glycerol and 2% glucose was achieved. MOF nanoparticles were coated by chiosan and characterized by DLS. TEM results, confirmed the spherical shape of the MOF with a porous center. In the MIC/MBC experiment against Pseudomonas aeruginosa by MOF-CS-CHAP(C) at concentrations of 4 and 8 ng/ml and in 24 to 48 hours, inhibition was observed. In the biofilm test, the concentration of 1,2,4,8ng/ml MOF-CS-CHAP(NC) nanoparticles on

Pseudomonas aeruginosa had the greatest effect on the biofilm. And in Staphylococcus aureus in MOF-CS-CHAP(C) and MOF-CS-CHAP(C) at all concentrations inhibition of biofilm formation was elicited. In Escherichia coli, in MOF-CS-CHAP(NC) and MOF-CS-CHAP(C) treatment at 8 ng/ml, it had the same effect on biofilm formation as Staphylococcus aureus. In evaluating the synergistic effect of vancomycin antibiotic with treatment groups, it had a significant effect on Staphylococcus aureus in both MOF-CS-CHAP(NC) and MOF-CS-CHAP(C) in 24 hours. A significant effect was observed in the synergistic effect of vancomycin antibiotic with CHAP protein in Pseudomonas aeruginosa at 24 and 48 hours.

Conclusion: The MOF-Chitosan nanoparticles conjugated with chimeric endolysin covalently and non-covalently can be an effective novel antibiotic against common infections.

Keywords: Chimeric protein, Antibiotic resistance, MOF-Chitosan, Gram positive and Gram negative bacteria

Synthesis and evaluation of β-amyloid aggregation inhibition of some benzothiazole derivatives using both experimental methods and molecular dynamic simulation method (Research Paper)

mohammad hossein asgarshamsi,[1,*] samira mahmoudi,[2]

1.
2. Department of Microbial Biotechnology, School of Biological Sciences, Islamic Azad University Tehran North Branch, Tehran, Iran.

Introduction: some novel inhibitors based on the (benzo[d]thiazol-2-yl)-1-phenylmethanimine derivatives were designed to reduce the aggregation process in Alzheimer's disease (AD). These structures seem to mimic stilbene-like scaffold while the benzothiazole moiety "locks" the thioflavin T (ThT) binding site. Other inhibitors were designed based on 2-((benzo[d]thiazol-2-ylimino)methyl)-5-(benzyloxy)-1-methylpyridin-4(H)-one derivatives.

Methods: Benzo[d]thiazol-2-amine derivatives were prepared by the reaction of aniline derivatives with ammonium thiocyanate in the presence of bromine/acetic acid. Then, the reaction of synthesized amines with benzaldehyde derivatives and 5-(benzyloxy)-1-methyl-4-oxo-1,4-dihydropyridine-2-carbaldehyde gave the desired compounds. The plate reader-based fibrillation assay was carried out to evaluate the inhibition of Aβ aggregation. To clarify the interaction manner of the designed compounds with Aβ formation, molecular dynamic simulation (MD) was carried out.

Results: The biological evaluation proved 4a, 5a, 5b and 5c and 7e as the best pro-aggregator and inhibitor of the Aβ aggregation. MD elucidated that the Aβ aggregation inhibitors in different concentrations represented different binding conformations throughout the entire or in one region of Aβ.MD simulation showed the ligands in lower concentrations accumulate in a region of Aβ aggregations and separate one fibril from the aggregated Aβ. On the contrary, in higher concentrations the ligands tend to be located through the entire Aβ.

Conclusion: The results were valuable for designing of novel pro-aggregator or inhibitors of Aβ aggregation. Future Studies on the compound 5a can be useful for design of novel multi-target directed ligands (MTDL) for treatment of Aβ based diseases.

Keywords: Amyloid beta, Pro-aggregator, Aminobenzothiazole, Molecular dynamic simulation (MD).

Synthesis of green gold spherical nanoparticles using curcumin

(Research Paper)

Houshang Nemati,[1,*] Mohammad hosein Ghahremani,[2] Sayed Hamid Madani,[3] Alireza firoz,[4] Ghobad Mohammadi,[5] Mehri Nazeri,[6]

1. Fertility and Infertility Research Center, Health Technology Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran
2. Department of Pharmacology and Toxicology, Faculty of Pharmacy, Tehran University of Medical Sciences
3. Department of pathology, Faculty of medicine, Kermanshah University of Medical Sciences
4. Faculty of Pharmacy, Tehran University of Medical Sciences
5.
6. Fertility and Infertility Research Center, Health Technology Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran

Introduction: In recent years, due to the widespread applications of nanotechnology in various industries such as medicine, pharmaceuticals and health, there is a great tendency to use them. Among nanoparticles, metal nanoparticles such as gold have received much attention due to their unique electrical, magnetic and optical properties.

Methods: In the present study, the green method has been used to produce gold nanoparticles using curcumin. Nanoparticles were formed after treatment with HAuCl4 solution with different concentrations of plant extracts as reducing agent at different temperatures. UV-vis was used to detect the formation of nanoparticles and FT-IR was used to determine the functional groups. Using DLS analysis, the size of nanoparticles was determined and small spherical nanoparticles were formed.

Results: The FTIR technique is used to identify the active groups and the performance of gold nanoparticles with curcumin. -1370- 1240 and 720 cm - shows 1). The Zeta Sizer diagram shows the nanoparticle size of about 30-50 nm (Figure)

Conclusion: Gold nanoparticles are synthesized by physical, chemical and green methods. Green methods such as the use of plant extracts are environmentally friendly and are suitable for the synthesis of nanoparticles due to the reduction of costs and the absence of toxic substances. In the present study, the green method has been used to produce gold nanoparticles using curcumin.

Keywords: Nanoparticle, Curcumin, FTIR, Size

Synthesis of MIL-100 nanocarrier and loading of oxaliplatin anticancer drug on it (Research Paper)

Ensieh sadat Seyed Hossien,[1,*] Maryam BIKHOF,[2] Mitra Salehi,[3] Mohammad Yousefi,[4]

1. Department of biology - faculty of biological science -North Tehran Branch- Islamic Azad university- Tehran- Iran
2. Department of biology - faculty of biological science -North Tehran Branch- Islamic Azad university- Tehran- Iran
3. Department of biology - faculty of biological science -North Tehran Branch- Islamic Azad university- Tehran- Iran
4. Department of Biology, Yadegar-e-Imam Khomeini (RAH) Shahr-e-Rey Branch, Islamic Azad University, Tehran, Iran

Introduction: Introduction: Today, cancer is the second leading cause of death in the world. Despite the great advances that have been made in chemotherapy, researchers are still looking for ways to deliver more effective drugs to the tumor that reduce side effects by slowly releasing the drug. Oxaliplatin is a type of chemotherapy drug used to treat colorectal cancer, which forms an intracellular link between DNA strands that inhibits transcription, disrupts the cell cycle, and ultimately causes apoptosis and cell death. In this study, in order to release oxaliplatin in a controlled manner and increase the effectiveness of chemotherapy, the MIL-100 nanocarrier was introduced as a new class of porous, high-surface crystalline MOFs containing iron oxide (III) clusters are synthesized and after loading the drug on it, the percentage of loading was calculated.

Methods: Methods: In this study, first the synthesis of MIL-100 (Fe) was performed by hydrothermal method. The synthesis method is as follows: H2BTC (1.6235g) and FeCl3.6H2O (0.8403g) are dissolved in 30ml of distilled water, then HF (0.213ml) and HNO3 (0.163ml) are added after 30 minutes in the oven for 20 hours at 150 ° C, the precipitate is centrifuged for 4 minutes at 4000 rpm and washed several times with distilled water and ethanol. Then MIL-100 (Fe) was dried in an oven at 150 ° C for 6 hours, and finally the orange powder of MIL-100(Fe) was obtained. The resulting MIL-100 (Fe) sample was confirmed by FTIR and XRD spectroscopy. Then, the drug was loaded on the nanocarrier with a weight ratio of 0.1 to 1 in the PBS buffer by a homogenizer at room temperature and the loading percentage was calculated after drawing the standard oxaliplatin curve.

Results: Results: The interpretation of the FTIR spectrum confirmed the synthesis of MIL-100(Fe). As the peak in region 3420 is the tensile vibration related to OH, the peaks of 1590 and 1390 show asymmetric and symmetrical vibrations of the C-O band in the carboxyl group of the trimic acid bonding

agent. The peak 750 of the CH-benzene extinction vibration of the benzene ring in trimic acid and the peak of 550 indicate FEO. The XRD spectrum also shows the two main peaks 2 ϑ=4 and 2 ϑ =11 and confirmed the crystallinity of the synthesized nanocarrier. The results of UV absorption spectroscopy showed lambda max value of oxaliplatin at 257nm. Also, oxaliplatin loading percentage on MIL-100 was calculated 52%.

Conclusion: Conclusion: The results of the present study showed that MIL-100(Fe) nanoparticles can be used as an efficient drug carrier for loading and delivery of oxaliplatin to cancer cells.

Keywords: Keywords: MOF, MIL-100, oxaliplatin, drug delivery

Synthesis of novel cell-penetrating peptide as a carrier for MCF-7 cancer cell line (Research Paper)

Mahsima Heydari,[1] Mohsen Farhadpour,[2] Mohammad Hossein Sanati,[3] Zahra Azizi,[4] Amir Norouzy,[5,*]

1. National Institute of Genetic Engineering and Biotechnology
2. National Institute of Genetic Engineering and Biotechnology
3. National Institute of Genetic Engineering and Biotechnology
4. Tehran University of Medical Sciences
5. National Institute of Genetic Engineering and Biotechnology

Introduction: In recent years, the effective delivery of pharmaceutical agents or diagnostic compounds to cells is the challenge of biology and medical science. Cell-penetrating peptides (CPPs), also known as protein transduction domains (PTDs) or membrane translocating sequence, are mostly short (5-30 amino acids) cationic peptides. CPPs have been considered as useful and promising cargo carriers due to their potential to cell entry without in a non-toxic fashion [1]. They are capable of carrying a wide range of macromolecules such as plasmids, DNA, small interfering RNAs (siRNAs), drugs (such as anticancer drugs), nanoparticles, proteins, viruses, fluorescent or radioactive compounds for Intracellular imaging [2]. The CPPs can penetrate the cells via different pathways, including energy-independent direct penetration across Biological Membranes and energy-dependent endocytosis without substantial damage to cell membrane [3]. In this study, it is reported on the development of an effective delivery; a novel cell-penetrating peptide (CPP), which is used for in vitro testing.

Methods: The CPP for this experiment FAM-YYYYRRRR was designed and synthesized employing solid-phase peptide synthesis method using the Fmoc strategy. 5-FAM (5-Carboxyfluorescein) serves as a fluorescent probe. It is also used p-sulfonatocalix[4]arene (CX4) with the desired peptide to enhance cell penetration and inhibit aggregation. MCF-7 cells were incubated with different concentrations of the peptide and peptide/CX4 in the range of 0.1 and 10 µM. Flow cytometry and fluorescent imaging techniques were used to evaluate the uptake of peptides into cells.

Results: The results showed that the FAM-YYYYRRRR peptide passing through the cell membrane in a slight matter, while the FAM-YYYYRRRR/CX4 uptake was relatively higher by the MCF7 cells in different concentrations, which shows the CX4 assisting role in the penetration.

Conclusion: The CX4 reduced peptide aggregation and eliminated the cytotoxicity effect. Therefore, it is suggested that the presence of the CX4

along with the peptide expedite peptide penetration into the cells in various concentrations of CPPs.

Keywords: MCF7, cancer cell, Cell-penetrating peptides, amphipathic peptide, p-sulfonatocalix[4]arene

Synthesis of UiO-66 nanoparticles containing Paclitaxel for lung cancer treatment (Research Paper)

Hanieh Jafari,[1] Maryam Bikhof Torbati,[2,*] Ahmad Majd,[3] Mohammad Yosefi3,[4]

1. Department of biology- faculty of biological science-Azad university- North Tehran Branch- Tehran- Iran
2. Department of Biology, Yadegar-e-Imam Khomeini (RAH) Shahr-e-Rey Branch, Islamic Azad University, Tehran, Iran
3. Department of biology- faculty of biological science-Azad university- North Tehran Branch- Tehran- Iran
4. Department of Chemistry, Faculty of Pharmaceutical Chemistry, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

Introduction: Metal-Organic Frameworks (MOFs) are emerging as suitable candidates for nanoscale drug delivery due to their high drug carrying capacity and ease of operation. The nanoporous UiO-66 as a kind of MOFs is attract for loading of one cargo molecule in drug delivery with very high surface area, excellent biocompatibility and chemical modifiability. Paclitaxel is an anti-proliferative drug and widely used for the treatment of non-small cell lung cancer. Paclitaxel binds to microtubules and inhibits microtubule depolarization during mitosis due to cell death. In this study, in order to reduce the unwanted side effects and the controlled release of paclitaxel and increase the effectiveness of chemotherapy, UiO-66 nanoparticles were synthesized and loaded with paclitaxel for the application in lung cancer treatment.

Methods: UiO-66 was synthesized by a solvent thermal method. In brief, 1.165 g of ZrCl4 and 0.831 g of BDC were dissolved in 30 mL DMF, and then 0.8 mL of concentrated HCl (37%) was added. The obtained mixture was ultrasouned in a reactor for 20 min and heated in a Teflon-lined steel autoclave at 120◦C temperature for 24 h duration time. The obtained suspension of UiO-66 was cooled and centrifuged at 9000 rpm for 10 min. Then the residue was washed three times with 25 mL of DMF and 25 mL of anhydrous methanol, respectively. The obtained UiO-66 was dried at 100 ◦C under vacuum and characterized by IR spectroscopy and X-ray powder diffraction (XRD). Then the loading of paclitaxel was performed on the UiO-66 nanocarrier in ethanol buffer with a weight ratio of 0.1 to 1 (drug/nanocarrier) by hemogenizer for 30 min. The Drug-loading content was calculated after drawing the standard paclitaxel curve by UV/visible spectroscopy- based assay.

Results: The FTIR spectra of UiO-66 display the peaks at 1700 cm−1 and 1400 cm−1 correspond to the symmetrical stretching vibrations of the C=O bond in the -COO- group, at 1506 cm−1 and 1581 cm cm-1 are assigned to

the C=C stretching vibration of the phenyl ring. Also, the peak at 745 cm-1 is consistent with the symmetric vibration peak of O-Zr-O and the symmetric vibration peak of O-Zr-O at 663 cm-1. Finally, these results confirmed the synthesized UiO-66. The drug-loading efficiency was calculated and showed high paclitaxol-loading content up to 57% on UiO-66.

Conclusion: In this investigation, we succeeded in effective loading of paclitaxol on the UiO-66 nanocarrier due to controlled drug delivery in cancer treatment .

Keywords: UiO-66, Paclitaxel, drug delivery, cancer

Tardigrades Model Animals Tolerant To Varios Extreme Environments (Review)

Niloofar Torkzadeh,[1,*] Mozhgan shirazi,[2]

1. Department of Biochemistry, Islamic Azad University, Falavarjan,Iran
2. Department of Biology, Scince and Reserch Branch, Islamic Azad University, Tehran, iran

Introduction: Extremphiles are organisms that have adapted or least tolerant to extremely harsh environments. Most Extremophiles are single organisms with simple structure, such as archaea and bacteria. However, some animals also exhibit extraordinary tolerance against extreme environment. One of the most known example of such extremotolerant animals is the tardigrade.

Methods: Extremphiles are organisms that have adapted or least tolerant to extremely harsh environments. Most Extremophiles are single organisms with simple structure, such as archaea and bacteria. However, some animals also exhibit extraordinary tolerance against extreme environment. One of the most known example of such extremotolerant animals is the tardigrade.

Results: tardigrades, also known as water bear, are tiny aquatic animals having four pairs of legs. More than 1.000 speceies have been reported from various habitats such as marine, fresh water or limno_ terrestrial environments. All tardigrades require surrounding water to grow and reproduce, but some limn_terrestrial species are able to tolerate almost complete dehydration. When the surrounding water evaporates, tolerant tardigrades lose almost all body water and enter a metabolically in active dehydrated called anhydroiosis. Genomic DNA stores all genetic information and is in dispensable for maintenance of normal cellular activity and propagation. Radiation causes severe DNA lesion, including double_strand breaks, and leads to genome instability and even lethality. Regardless of the toxicity of radiation, some organisms exhibit extraordinary tolerance against radiation. These organisms are supposed to possess special mechanisms to mitigate radiation_induced DNA damages. Here we deter mine a nigh quality genome sequence of Ramazzottius varieornatus on of the most strees tolerant tardigrade spece. R.varieornatus is one of the most radiotolerant speciesin tardigrades. Considering DNA as a major target of radiation damage, the tardigrade is assumed to possess some protein associated with DNA to protect and/ or effectively repair DNA. Recently, as a representative of such proteins, damage suppressor (DSUP) Was identified from a chromation fraction of the tardigrade. In this review, we summarized the current know ledgs of extremely radiotilerant animals, mainy focusing on tardigrades as an emerging animal model of extremophiles. Antioxidant defenses and the efficient DNA rapair by protected enzymes have been accepted as a common

basis for elevated radiotolerance shared from prokaryotes to animals. The recent genome analyes revaled that tardigrades also possess redundant copies of antioxidant enzymes and DNA repair enzymes while lacking ROS-producing enzymes, so a similar principle could be applicable to tardigrades as well. Although the precise mechanism of DNA protection by DSUP protein remain to be elucidated, the association with DNA is important for protection activity of DSUP protein, suggesting a possible physical shielding of DNA from ROS and irradiation and/or a local detoxification of ROS as potential mechanisms.

Conclusion: minor change in the gene expression profiles during dehydration and rehydration suggest constitutive expression of tolerance related gene. The findings indicate the relevance of tardigrade unique proteins to tolerability and tardigrades could be a bountiful source of new protection genes and mechanism.

Keywords: Tardigrade, Genomic, Radiotolerance, Damage Suppressor(DSUP), Space Biology

Targeting genes of Hsp90 and hTERT by 17-DMAG loaded PLA/PEG electrospun nanofibrous scaffolds in T47D breast cancer cells (Research Paper)

Hasan Mellatyar,[1,*] Sona Talaei,[2]

1. Department of Basic Sciences, Maragheh University of Medical Sciences, Maragheh, Iran
2. Department of Basic Sciences, Maragheh University of Medical Sciences, Maragheh, Iran

Introduction: Up-regulation of Hsp90 and hTERT genes takes place in breast cancer cells, and their targeting may be a promising step in breast cancer therapy. In this study, poly(lactide)-poly(ethylene glycol) (PLA-PEG) nanofibers loaded with 17-dimethylaminoethylamino-17-demethoxy geldanamycin (17-DMAG) were designed to increase the anti-cancer effect of 17-DMAG.

Methods: For this purpose, 17-DMAG-loaded PLA-PEG nanofibers were successfully fabricated via electrospinning technique and characterized using Field Emission Scanning Electron Microscopy (FE-SEM) and Fourier Transform Infrared (FTIR). Colorimetric MTT metabolic activity assay was used to determine the drug cytotoxicity. Also, the expression levels of the Hsp90 gene in the T47D cells seeded on the scaffolds were assessed using real-time RT-PCR. The effect of 17-DMAG and 17-DMAG loaded PLA-PEG nanofiber treatment on telomerase activity was monitored by TRAP assay.

Results: Taking into account drug load, IC50 has significantly reduced in 17-DMAG-loaded PLA-PEG nanofibers than free 17-DMAG. This finding was associated with a decrease in Hsp90 gene expression and telomerase activity.

Conclusion: 17-DMAG-loaded PLA-PEG nanofibers can be more effective than free 17-DMAG in down-regulating the Hsp90 expression and inhibiting the activity of telomerase, at the same time exerting more potent cytotoxic effects. Therefore, PLA-PEG can be a superior carrier for this type of hydrophobic agent.

Keywords: Breast Cancer, Hsp90, 17-DMAG, PLA/PEG nanofiber, hTERT.

Targeting Hsp90 gene expression by 17-AAG-loaded PLGA/PEG nanoparticles in lung cancer cells (Research Paper)

Sona Talaei,[1,*] Hasan Mellatyar,[2]

1. Department of Basic Sciences, Maragheh University of Medical Sciences, Maragheh, Iran
2. Department of Basic Sciences, Maragheh University of Medical Sciences, Maragheh, Iran

Introduction: Hsp90 is overexpressed in cancer cells that are considerably dependent on the function of Hsp90. 17-allylamino-17-demethoxygeldanamycin (17-AAG) inhibits Hsp90 expression and function. 17-AAG has weak water solubility, which is a possible problem for its clinical application. In this study, poly (lactic acid-co-glycolic acid)-poly (ethylene glycol) (PLGA-PEG) nanoparticles are used for improving the stability and solubility of 17-AAG in drug delivery systems.

Methods: Encapsulation of 17-AAG was performed by the double emulsion method, then the amount of loaded drug was calculated. 17-AAG-loaded PLGA-PEG nanoparticles are characterized using H nuclear magnetic resonance (HNMR) and Fourier Transform Infrared (FTIR). For assessing cytotoxicity of PLGA-PEG nanoparticles loaded with 17-AAG on the grown of lung cancer cells, the colorimetric cell viability (MTT) assay was used. Cells were treated with equal concentrations of free 17-AAG and 17-AAG-loaded PLGA-PEG nanoparticles, and Hsp90 gene expression levels in the two groups were compared by real-time PCR.

Results: Regarding the amount of 17-AAG load, IC50 was significantly reduced in cells treated with nanoencapsulated 17-AAG compared to free 17-AAG. This result was confirmed by the decrease of Hsp90 gene expression by real-time PCR.

Conclusion: The results demonstrated that PLGA-PEG-17-AAG complexes are more effective in comparison with free 17-AAG for down-regulating of expression of Hsp89 by increasing uptake by cells. Therefore, PLGA-PEG can be a superior carrier for this kind of hydrophobic agent.

Keywords: Lung Cancer, Hsp90, 17-AAG, PLGA-PEG, Nanoparticle.

Targeting microRNAs by curcumin: implication for cancer therapy (Review)

Fatemeh Sadoughi,[1] Parisa Maleki Dana,[2] Zatollah Asemi,[3] Bahman Yousefi ,[4,*]

1. Research Center for Biochemistry and Nutrition in Metabolic Diseases, Institute for Basic Sciences, Kashan University of Medical Sciences, Kashan, Iran.
2. Research Center for Biochemistry and Nutrition in Metabolic Diseases, Institute for Basic Sciences, Kashan University of Medical Sciences, Kashan, Islamic Republic of Iran.
3. Research Center for Biochemistry and Nutrition in Metabolic Diseases, Institute for Basic Sciences, Kashan University of Medical Sciences, Kashan, Iran.
4. Department of Biochemistry, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.

Introduction: Curcumin is a polyphenol that has been widely used in the cancer treatment field due to its several beneficial effects, including anti-inflammatory impacts, apoptosis induction, and anti-oxidant processes. Moreover, curcumin is able to affect different signaling pathways, transcription factors, and growth factors. MicroRNAs are a subclass of small non-coding RNAs which are involved in regulating the expression of various genes by epigenetic processes, such as histone modification and DNA methylation. In recent years, changing the microRNAs' expression has attracted the attention of researchers as a new aspect of curcumin's beneficial effects in cancer therapy. Thus, herein, we investigate how curcumin modulates cancer hallmarks by involving microRNAs.

Methods: This study aims to collect the information available on the applications of curcumin in cancer therapy that are mediated by different microRNAs. Different search engines (e.g. PubMed and Google Scholar) have been used to find the relevant data and a summary of what we know so far has been provided.

Results: Research has shown that curcumin leads to cell cycle arrest and suppresses the proliferation in cancer cells through different microRNAs (such as miR-21, miR-192-5p, and has-miR-138). It is also reported that microRNAs (e.g. miR-182-96-183 and miR-181b) are involved in curcumin inhibitory effects on metastasis and invasion of cancer cells. MicroRNAs (e.g. miR 146a and miR-29b-1-5p) can also mediate the curcumin chemo-sensitizing effect which is important for overcoming chemo-resistance. Furthermore, a few studies are suggesting that curcumin may play a role in the DNA damage response of cancer cells by microRNAs.

Conclusion: Curcumin's ability to exert its antitumor effect through microRNAs leads to better opportunities of providing targeted therapies, reducing resistance against common chemotherapeutic agents, and decreasing adverse effects of common therapeutic approaches.

Keywords: curcumin, microRNA, cancer therapy, cancer hallmarks

The Antinociceptive Effect of Isoniazid in the Acetic Acid Writhing Test in Mice (Research Paper)

Amir Abbas Barzegari,[1,*] Maryam Azaddar,[2] Babak Vahdani,[3] Saeed Khalili,[4]

1. Assistant Professor of Animal physiology, Department of Biology, Faculty of Basics Sciences, University of Maragheh, Maragheh, Iran.
2. Instructor of Animal physiology, Department of Biology, Faculty of Basics Sciences, University of Maragheh, Maragheh, Iran.
3. Master of Science (MSc) student in Microbial Biotechnology, Department of Biology, Faculty of Basics Sciences, University of Maragheh, Maragheh, Iran.
4. Master of Science (MSc) student in Microbial Biotechnology, Department of Biology, Faculty of Basics Sciences, University of Maragheh, Maragheh, Iran.

Introduction: Many neurotransmitters in the central nervous system are involved in pain perception and modulation. Isoniazid, as an important anti-tuberculosis drug, is also a modulator of the GABAergic system in the CNS. As a result, the purpose of the present research was to evaluate the effects of isoniazid on the acetic acid writhing test (a non-selective animal model of pain) in mice.

Methods: Four groups of mice (n=8) were used in this study. In this study, the pain was induced by intraperitoneal injection of acetic acid (0.6%, 10 ml/kg) in mice. Saline or isoniazid at doses 25, 50, and 75 mg/kg was administered intraperitoneally 60 min before acetic acid administration. Then, the abdominal writhes were counted during a 30-min period of the test.

Results: Isoniazid in doses 25, 50, and 75 mg/kg decreased the number of writhes in the experimental groups compared with the saline-treated group. The dose of 75 mg/kg was the most effective dose of isoniazid in pain reduction.

Conclusion: In conclusion, isoniazid has an antinociceptive effect in the writhing test in mice.

Keywords: Isoniazid, Pain, writhing Test, Antinociceptive effect

The Application of CRISPR/Cas9 Technology for Editing MicroRNAs in Cancer Research (Review)

Sedigheh Sadat Mortazavi,[1] Sedigheh Gharbi,[2,*]

1. Division of Genetics, Department of Biology, Faculty of Sciences, Shahid Bahonar University of Kerman, Kerman, Iran.
2. Division of Genetics, Department of Biology, Faculty of Sciences, Shahid Bahonar University of Kerman, Kerman, Iran.

Introduction: As the second leading cause of death, cancers are still a significant public health problem, imposing a heavy financial burden on societies worldwide. Cancer is a multifactorial disease with diverse genetic and epigenetic alterations. As critical epigenetic regulators, microRNAs (miRNAs) are implicated in every step of cancer development. The clustered regularly interspaced short palindromic repeats (CRISPR)-associated nuclease 9 (CRISPR/Cas9) system has evolved as a revolutionary genome-editing technology with great potential to assist cancer therapies especially those related to non-coding RNAs. Moreover, increasing evidence has revealed that CRISPR/Cas9 genome editing technology can target small non-coding RNAs, such as miRNAs, and represent a novel strategy to modify their expression and function in diseases like cancers.

Methods: Two databases (PubMed and Google Scholar) were searched based on the selected keywords, including 'cancer' and 'CRISPR' and 'microRNA,' to identify relevant articles that described CRISPR/Cas9 technology application for editing miRNAs in various cancers. Obtained results were filtered from the year 2017 to 2021. After reviewing abstracts and finding related articles, we summarize information in several sections covering a brief review of CRISPR technology, its applications on tumor therapies, as well as modifying miRNAs in human cancers.

Results: After integrating information from the databases mentioned above, 65 articles were obtained for further investigations. Using CRISPR/Cas9 technology, scientists have shed light on miRNA functions in cancers, such as oncogenicity and drug resistance. For example, miRNAs play critical roles in the development of cancers. Recently scientists used CRISPR/Cas9 technology to introduce different mutations in the precursor sequence of oncogenic miRNAs and alter their biogenesis by Drosha/Dicer. Their results demonstrated a reduction in the expression of oncogenic miRNA and eventually inhibition of proliferation and invasion of the cancer cells.

Conclusion: MiRNAs could serve as novel diagnostic markers and therapeutic targets in cancers. Therefore, the combination of CRISPR/Cas9

genome-editing technology with miRNA therapeutics can improve the understanding of the cancer nature and eventually hold immense therapeutic promise for cancer patients.

Keywords: Cancer, miRNA, CRISPR, Therapy.

The association between first trimester maternal serum PAPP-A levels and some pregnancy outcomes (Review)

Samane Zeynodini,[1,*]

1. Department of nursing and midwifery, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

Introduction: Pregnancy associated plasma protein A (PAPP-A) is a protein mostly produced by placenta. It is one of the components of first trimester combined test which is an effective test for predicting fetal chromosomal anomalies. Some studies have shown an association between PAPP-A and some pregnancy outcomes. In due to measuring maternal serum PAPP-A levels in first trimester, it can be a predictive factor for complications which is associated with it. The aim of this review is to check out studies been published about PAPP-A relationship with some pregnancy outcomes.

Methods: A review literature search of eligible studies was conducted in the PubMed database from 2015 to 2021 for studies evaluating the association PAPP-A and some maternal outcomes using the following search strategy : ("Pregnancy associated plasma protein A " OR "PAPP-A") AND ("pregnancy outcome") as used keywords. 21 studies (meta-analysis) were found and 10 studies were included in this review.

Results: Two studies have reported the relationship between PAPP-A and Gestational diabetes Mellitus (GDM).On top of that one of them showed that the predictive value of PAPP-A for GDM has 55% sensitivity, 90% specificity with 95% confidence intervals. In another meta-analyze study PAPP-A <5th centile had a moderate association with pre-eclampsia OR 1.94 and preterm birth <37 weeks OR 2.09 was reported, however the predictive value was poor.

Conclusion: First trimester low maternal serum PAPP-A has an association with GDM, pre-eclampsia and preterm birth, however the predictive values of PAPP-A itself is poor so further works around combining this factor with others seem to be necessary.

Keywords: Pregnancy associated plasma protein A , PAPP-A, pregnancy outcome

The association between serum estradiol level and stress score and sexual function in women admitted to a Tehran level 3 hospital for Corona disease (Research Paper)

Elahe Sadeghi Sahebzad,[1] Najmeh Tehranian,[2,*] Anoshirvan Kazemnejad,[3] Mohsen Sharifi,[4] Faraz Mojab,[5]

1. Department of Reproductive Health and Midwifery, Faculty of Medical Sciences, Tarbiat Modares University
2. Department of Reproductive Health and Midwifery, Faculty of Medical Sciences, Tarbiat Modares University
3. Department of Biostatistics, Faculty of Medical Science, Tarbiat Modares University
4. Department of Plant Biology, Tarbiat Modares University
5. School of Pharmacy and Pharmaceutical Sciences Research Center, Shahid Beheshti University of Medical Science

Introduction: Sexual function is a part of human life and behavior and is a multidimensional phenomenon that is influenced by a variety of biological, psychological, and social factors.. Estradiol is one of the hormones that is directly related to the level of sexual function. Coronary heart disease causes severe mental and physical stress which may result in reduced sexual function

Methods: This correlational study was performed in 2021 on 223 pregnant women with a history of fetal or neonatal death referred to the gynecology clinic of Shohada Yaftabad Hospital (Level 3 Corona Hospital) by convenience sampling method. The women underwent venous blood sampling in the follicular phase and then completed the demographic characteristics (including personal information), the Sexual Function (FSFI), and the DOS Stress Questionnaire. Data were analyzed using SPSS software version 21

Results: According to the Pearson correlation test, the mean of the total score of sexual function had a significant inverse correlation with stress ($p < 0.001$ $r = 0.983$). In other words, the more stress, the lower the score of sexual function. Also, based on this test, it was found that estradiol levels have a positive correlation with sexual function ($p = 0.001$ $r = -0.23$)

Conclusion: According to this research, the stressful conditions established in the community as a result of the corona pandemic result in a multitude of issues with sexual function and estradiol levels.

Keywords: Estradiol, Sexual function, stresss

The association between tobacco and Covid-19 (Review)

Ali salimi asl,[1] Elham Yadegarifard,[2,*] Narjes Seddighi,[3] maryam mabani,[4] amin reza nikpoor,[5]

1. Student Research Committee, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
2. Student Research Committee, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
3. Student Research Committee, Faculty of Para-Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
4. Department of Immunology, Faculty of Medicine, Hormozgan University of Medical Science, Bandar Abbas, Iran.
5. Department of Immunology, Faculty of Medicine, Hormozgan University of Medical Science, Bandar Abbas, Iran.

Introduction: SARS CoV-2 virus is the cause of COVID-19 disease. The first case of the disease was found in China in early December 2019, and over time it has spread around the world, causing the COVID-19 pandemic. The disease is mainly related to the respiratory system, causes severe acute respiratory infections and is associated with unprecedented high mortality. Smoking endangers the immune system and affects almost all parts of the body, increasing the chances of developing a respiratory infection (such as a viral infection), severe illness, and hospitalization and it is a risk factor for common chronic diseases. Due to the fact that tobacco can have adverse effects on body systems, the aim of this study was to investigate the effects of tobacco on the incidence, transmission, prognosis and severity of the disease in Covid-19 patients.

Methods: Article selection were conducted through advanced search in science direct, Pubmed, google scholar database and without time limit, using three keywords derived from MeSH (Covid-19, smoking, tobacco) and limiting the search to keywords in the title and abstract. From the 97 available articles based on the content of the abstracts, 46 articles were selected. The articles were studied and key points of each were identified.

Results: Covid-19 virus can infect various systems of the body. The most important system that is damaged during this disease is the respiratory system, which in severe cases leads to pneumonia and ARDS. The virus also affects the cardiovascular system, causing coronary artery obstruction and can affect the gastrointestinal, renal and nervous systems. Cigarettes are composed of more than 7,000 toxic chemicals and smoking and exposure will lead to disease such as cancer, pneumonia, cardiovascular diseases, etc by affecting various systems of the body (respiratory system, cardiovascular system, urinary and renal system, digestive system and nervous system).

according to the WHO, smokers are more exposed to the disease by increasing hand-to-mouth contact and increasing the risk of transmitting the virus. Many studies show that the incidence of Covid-19 in patients with active smoking was much lower than in patients with no history of smoking. This may be due to the presence of nicotine in cigarettes, which has an inhibitory effect on proinflammatory cytokines and plays an important role in the Pathophysiology of Covid-19 disease. However, more studies are needed to investigate the effect of tobacco, cigarette and their contents on the incidence of Covid-19 disease. The results of various studies show that smoking, by affecting the prognosis and outcome of Covid-19 disease, increases the severity of the disease, the need for hospitalization and ICU, as well as the death rate and challenges treatment. Covid-19 has changed the attitude and idea of smokers towards tobacco; so that most studies show that people are more tendency to quit tobacco.

Conclusion: According to the results of various studies, smokers are less likely to develop COVID-19 disease, but the rate of transmission, disease severity, death, and the need for hospitalization in smokers has increased, making treatment challenging. Therefore, since smoking can increase the severity of the disease, it can be concluded that smoking and cigarette cessation can help improve the function of the respiratory system.

Keywords: Covid-19, smoking, tobacco, cigarette

The association of PPARγ expression pattern with pathophysiology and inflammatory status of malignant bone tumors (Research Paper)

Amir Reza Eghtedari,[1] Banafsheh Safizadeh,[2] Mohammad Amin Vaezi ,[3] Khodamorad Jamshidi,[4] Masoumeh Tavakoli-Yaraki ,[5,*]

1. Department of Biochemistry, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
2. Department of Biochemistry, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
3. Department of Biochemistry, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
4. Bone and Joint Reconstruction Research Center, Shafa Orthopedic Hospital, Iran University of Medical Sciences, Tehran, Iran
5. Department of Biochemistry, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.

Introduction: Primary bone and joint malignancies are the third leading cause of death in cancer patients under 20 years of age. The handling of bone tumors is considered a big challenge for oncologists and surgeons due to their diverse histological natures and different clinical manifestations. Therefore, early detection of either recurrent or metastatic disease can contribute to timely decisions and action to treat the tumor, improving patient prognosis. In the present study the expression pattern of PPARγ and its relevance to the inflammatory cytokines (IFNG, TGFB) were assessed in malignant bone tumors at protein level and the relevance of the its expression level with patient's clinic pathophysiology were evaluated.

Methods: In this case-control study, 90 patients with osteosarcoma and Ewing sarcoma bone tumors from Shafa yahyaeen hospital were enrolled in the study. The tumor, normal bone tissues and serum of patients were collected and the protein level of PPARγ was assayed via immunohistochemistry and the level of IFNG, TGFB were assessed using ELISA.). Side-to-side comparisons were conducted using the parametric unpaired t-test and nonparametric Mann–Whitney U test. The chi-square test was used to analyze the statistical differences between bone tumors and the variables (age, gender, tumor grade, tumor size, metastasis, chemotherapy status, response to therapy and tumor recurrence).

Results: Measurement of PPARγ expression level in tumor tissues of patients with malignant bone tumors revealed that its level was significantly increased in patients comparing to normal tissues. Also, the increased levels of IFNG, TGFB were detected in serum of patients with malignant bone tumors compared to healthy controls which was associated with elevated level of PPARγ in tumor tissues. The association was observed regarding the level of

PPARγ, IFNG and TGFB with tumor grade, metastasis and response to therapy.

Conclusion: Our data provide a more efficient and accessible picture of PPARγ expression pattern in bone cancer and further pieces of evidence to utilize it as a possible diagnostic marker in bone tumor pathogenesis.

Keywords: PPARγ, malignant bone tumors, cancer, inflammation

The benefit of surface coating with adipose tissue-derived mesenchymal stem cells on the survival and function of pancreatic islets (Research Paper)

Mona Navaei-Nigjeh,[1,*] Marzieh Daniali,[2] Soheyl Mirzababaei,[3]

1. Pharmaceutical Sciences Research Center (PSRC), The Institute of Pharmaceutical Sciences (TIPS), Tehran University of Medical Sciences, Tehran, Iran
2. Pharmaceutical Sciences Research Center (PSRC), The Institute of Pharmaceutical Sciences (TIPS), Tehran University of Medical Sciences, Tehran, Iran
3. Pharmaceutical Sciences Research Center (PSRC), The Institute of Pharmaceutical Sciences (TIPS), Tehran University of Medical Sciences, Tehran, Iran

Introduction: Pancreatic islets, especially the large islets have poor survival rates in culture. Co-culturing with mesenchymal stem cells (MSCs) has been shown to improve islet survival and function. However, most co-culture studies have been comprised of MSC surrounding islets in the media. The present study aimed to develop technique for surface coating of islets with adipose tissue-derived MSCs (AT-MSCs) in order to investigate survival and function such bioengineered islets.

Methods: Pancreatic islets and AT-MSCs isolated from Wistar rats were incubated at 37°C for 1 h during gentle shaking and then cultured without shaking for 4 days. The survival and function of islets were measured morphologically and by analyzing insulin secretion in response to glucose challenge.

Results: Coating pancreatic islets with AT-MSCs showed improved islet survival after 4 days of culture. In addition, AT-MSCs-coated islets revealed preserved function with higher insulin secretion compared with control-native islets.

Conclusion: We conclude that bioengineering of islets with AT-MSCs may be useful for potentiating pancreatic islets' functionality and feasibility. Accordingly, the technique presented allows for pretreatment of donor islets with recipient-derived MSCs as a means of improving islet engraftment.

Keywords: Adipose tissue, Islet transplantation, Mesenchymal stem cells, Pancreatic islets, Surface coating

The carbon quantum dots-disulfiram conjugate via disulfide bonding for targeted drug delivery (Research Paper)

Mohamad Mahani,[1,*] Mohadese Panaei,[2] Faeze Khakbaz,[3] Mehdi Yousefian,[4]

1. Department of Chemistry, Faculty of Chemistry and Chemical Engineering, Graduate University of Advanced Technology, Kerman, Iran.
2. Department of Chemistry, Faculty of Chemistry and Chemical Engineering, Graduate University of Advanced Technology, Kerman, Iran.
3. Department of Chemistry, Shahid Bahonar University of Kerman, Kerman, Iran
4. Department of Chemistry, Faculty of Chemistry and Chemical Engineering, Graduate University of Advanced Technology, Kerman, Iran.

Introduction: Disulfiram (DSF) has been used as an anti-alcoholism drug for over 60 years [1]. Plenty researches have shown evidence of promising anticancer efficacy of this agent for treatment of wide range of cancers [2]. nanoparticles can improve DSF solubility, isolate it from labile environment and enhance its accumulation in the tumor tissue, which altogether result in a better anticancer efficacy [3]. As a group of newly emerged fluorescent nanomaterials, Carbon quantum dots (CQDs) have shown tremendous potential as versatile nanomaterials for a wide range of applications, including biosensing, bioimaging and drug delivery [4]. CQDs is an important carbon nano-material with dimensions less than 10 nm, comprising of amorphous or crystalline center with an oxidized carboxylic carbon surface [5]. In this paper, the CQDs-DSF conjugate was investigated for targeted drug delivery.

Methods: First citric acid and urea were dissolved in DMSO. This solution was transferred into autoclave and incubated at 160c for 4 h in an oven. The resulting solution was dark brown in color due to the formation of the CQDs. Then CQDs were diluted with distilled water, DTT was added and stirred to activate the sulfur functional group. The DSF was added to sulfur functionalized CQDs and stirred for 24 h.

Results: The absorption spectra of CQDs were recorded in the UV-Vis region. The absorption peak at nearly 250 nm can be attributed to the π -π* transitions and the peak observed at 350 nm can be attributed to n-π* transitions. The absorption spectrum of DSF was also observed at 280 nm. The highest fluorescence emission of CQDs intensity is related to the emission wavelength of 460 nm in excitation wavelength of 365 nm. The particle size of CQDs was obtained 3 nm .The surface functional groups of the CQDs were detected using the FTIR. A broad band is observed from 2800 to 3500 cm−1, showing the presence of N−H and O−H bonds and thereby confirming the presence of N in the CQDs. The sharp peak at 1632 cm−1 can be due to the c=o groups. The peak around 1205cm-1 is ascribed to the C–O,

C–N, and C–S bonds. The percent loading of the drug was calculated 34%. The release drug in the presence of glutathione (GSH) at pH=5.4 was show an upward trend and reached 80% after 24 h In this study CQD was exhibit no cytotoxic effect and free DSF was show lower cell viability effect. The cytotoxicity of CQDs-DSF was lower in comparison with CQDs-DSF-GSH.

Conclusion: In this study, the solvothermal method was used to synthesize CQDs. The CQDs were biocompatible because it showed no cytotoxicity in MCF-7 cells so can be used as an efficient nanocarrier. With increasing concentration of CQD-DSF cell death also increases, with the difference that an increase in cell death is more observed in the presence of glutathione because glutathione breaks disulfide bonds and releases more drug. Glutathione amount is different in normal and cancer cells. As a result, targeted drug delivery can be performed in the presence of glutathione.

Keywords: Carbon quantum dot, Disulfiram, Drug delivery

The clinical significance of MMP-9 protein level in patients with primary malignant bone tumors and its association with tumor severity, metastasis and response to chemotherapy. (Research Paper)

Mohammad Amin Vaezi,[1] Banafsheh Safizadeh,[2] Amir Reza Eghtedari,[3] Khodamorad Jamshidi,[4] Masoumeh Tavakoli-Yaraki ,[5,*]

1. Department of Biochemistry, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.
2. Department of Biochemistry, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.
3. Department of Biochemistry, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.
4. Bone and Joint Reconstruction Research Center, Shafa Orthopedic Hospital, Iran University of Medical Sciences, Tehran, Iran
5. Department of Biochemistry, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.

Introduction: Primary bone tumors are considered as non-frequent mesenchyme-originated solid tumors which affected individuals at all age ranges. The dynamic of bone tissue-dependent to the tissue physiological and pathological condition which makes it susceptible to cellular re-arrangement, tumor cell formation, and tumor cell implantation. Despite recent improvements regarding primary bone tumor diagnosis and therapeutic strategies, still nonspecific symptoms besides late patient referring and early detection failing are prominent drawbacks that cause cancer-induced morbidity and mortality. In the present study the expression pattern of MMP9 and its relevance to the biochemical profile and tumor pathophisiology were assessed in malignant bone tumors.

Methods: The number of 90 bone tumor tissues, 90 tumor margins, and 90 peripheral bloods taken from the same patients with bone tumor were enrolled in the current study with local ethical approval and informed consent. The MMP-9 expression level (protein) was evaluated using immunohistochemistry and the biochemical profile of the patients were assessed using ELISA and calorimetry. Side-to-side comparisons were conducted using the parametric unpaired t-test and nonparametric Mann–Whitney U test. The chi-square test was used to analyze the statistical differences between bone tumors and the variables (age, gender, tumor grade, tumor size, metastasis, chemotherapy status, response to therapy and tumor recurrence).

Results: The elevated level of MMP-9 expression was detected in bone tumors and malignant tumors compared to normal tissues. Tumor grade, size, metastasis, recurrent and the level of response to chemotherapy showed correlation with the MMP-9 protein level in malignant bone tumors. The

simultaneous overexpression of MMP-9 in tumor tissues was more prominent in malignant bone tumors and correlated with tumor size, grade, metastasis, recurrent, and response to chemotherapy.

Conclusion: Our data emphasize the possible involvement MMP-9 as a mediator and a potential diagnostic biomarker in primary bone cancer.

Keywords: MMP-9, malignant bone tumors, cancer, metastasis.

The combined effect of Pdx1 overexpression and Shh manipulation on the function of insulin-producing cells derived from adipose-tissue stem cells (Research Paper)

Dian Dayer,[1,*] Mohammad Reza Tabandeh,[2] Mahmud Hashemi Tabar,[3] Eskandar Moghimipoor,[4]

1. Cellular and Molecular Research Center, Medical Basic Sciences Research Institute, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
2.
3. Department of Anatomy, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
4. Department of Pharmaceutics, Faculty of Pharmacy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Introduction: Pancreatic and duodenal homeobox 1 (Pdx1) and Sonic hedgehog (Shh) are the key regulators of beta-cell function. In vitro experiments have shown that there is significant cooperation between Pdx1 and Shh with regard to the production and maintenance of insulin-producing cells (IPCs). In this study, the combined effect of Pdx1 overexpression and Shh manipulation on the function of adipose tissue-derived IPCs was determined.

Methods: A eukaryotic expression vector (Pdx1-pCDNA3.1(+)) was constructed and transfected into a Chinese hamster ovary (CHO) cell line. Adipose tissue-derived mesenchymal stem cells (ADMSCs) obtained from rats were assigned to two groups [control (C) and manipulated (M)] and differentiated into IPCs. Manipulated cells were treated with a mixture of FGF-b and cyclopamine and recombinant Shh protein at days 3 and 11, respectively, and transfected with Pdx1-pCDNA3.1(+) at day 10. The expression of multiple genes related to function of beta cells was analyzed using real-time PCR. The functionality of IPCs in vitro was analyzed through dithizone (DTZ) staining and ELISA. IPCs were injected into the tail vein of diabetic rats, and blood glucose and insulin concentrations were measured.

Results: CHO cells transfected with Pdx1-pCDNA3.1(+) showed a significantly higher expression of Pdx1 compared with nontransfected cells. Manipulated IPCs exhibited a significantly higher expression of MafA, Nkx2.2, Nkx6.1, Ngn3, insulin, and Isl1 and a higher insulin secretion in response to glucose challenge in relation to control cells. Rats that received manipulated IPCs exhibited a higher ability to normalize blood glucose and insulin secretion when compared to controls.

Conclusion: Our protocol might be used for more efficient cell therapy of patients with diabetes in the future.

Keywords: adipose tissue-derived mesenchymal stem cells; insulin-producing cells; Pdx1; sonic hedgehog pathway

The combined reducing effect of saffron and resistance training on blood pressure in the elderly hypertensive men (Research Paper)

Shima Mojtahedi,[1,*] Babak Hooshmand Moghadam,[2]

1. Faculty of Physical Education and Sport Sciences, between 15th and 16th St., North Kargar st., Tehran, Islamic Republic of Iran
2. Department of Exercise Physiology, Faculty of Sport Sciences, Ferdowsi University of Mashhad, Mashhad, Iran.

Introduction: Hypertension, predominant over other risk factors such as diabetes and improper lifestyle and nutrition, is one of the leading causes of death among patients suffering from cardiovascular diseases, especially among middle-aged and older adults in the world. The use of natural therapeutic approaches, such as physical activity and herbs, can help treat this disease. However, we aimed to determine the independent and combined effects of saffron and resistance training on blood pressure (BP) and some biochemical markers in the elderly with hypertension.

Methods: The present study was a randomized clinical trial on hypertensive men aged 60-70 years who were assigned to a control group (CO) and three experimental groups; resistance training (RT), saffron (S) and resistance training + saffron (RTS) for 12 weeks. Patients in S and RTS received one tablet containing 200 mg of saffron daily. BP variables, chemical biomarkers, and anthropometric indicators, were measured at weeks 0, 6, 12, and 18. Data were analyzed by repeated measurements analysis of variance (ANOVA).

Results: In comparison to the CO ($P<0.001$) and S ($P=0.01$), RTS reduced systolic blood pressure. Nitric oxide (NO) increased in the RTS compared to the CO group ($P=0.001$). There was a significant increase and decrease in adiponectin and endothelin-1 in the S ($P=0.012$) ($P<0.001$) and RT ($P<0.001$) ($P=0.003$) compared to the CO respectively. There was no significant difference between the groups for ANP.

Conclusion: Resistance training and consumption of saffron can improve blood pressure in the elderly with hypertension by affecting the factors involved in altering vascular endothelial resistance.

Keywords: saffron, resistance training, hypertension, elderly men

The effect of antibacterial factors of Diospyros lotus leaf and fruit extract on pathogenesis: A review study (Review)

Alam Ara Gholami,[1] Ali Ahmadi ,[2,*]

1. Assistant Professor, Department of Biological Sciences and Technologies, Islamic Azad University, Sari Branch, Sari, Iran
2. Student, Department of Biological Sciences and Technologies, Islamic Azad University Sari Branch, Sari, Iran

Introduction: Persimmon genus with the scientific name of Ibnaseh has 6 genera and 300-400 species. In the natural habitats of Iran, the genus Essence has only one genus called Diospyros lotus with two species, which include: Diospyros lotus and Diospyros tomatoes. This study aimed to investigate the effect of antibacterial agents of Diospyros lotus leaf and fruit extract on pathogenesis bacteria.

Methods: This review study was conducted in 2021 by searching for keywords such as antibacterial agents, Diospyros lotus, plant extracts, and pathogenesis microorganisms invalid databases.

Results: Based on the study of various articles, the results show that today, the use of multiple antibiotics due to lack of proper diagnosis, causes the emergence of more than one type of antibiotic-resistant in the patient. On the other hand, it should be noted that the limited duration of an antibiotic can be used as the drug of choice for the treatment of infections caused by resistant bacteria.

Conclusion: According to the results of the mechanism, the protective effect is related to the presence of antioxidant compounds such as flavonoids and naphthocytones in the plant, which neutralizes the toxic and radical composition of the pyrrolizidine alkaloid Sensivulgaris.

Keywords: Antibacterial agents, Diospyros lotus and pathogenesis microorganisms

The effect of Azacitidine and Trichostatin A on impaired osteogenic differentiation capacity of bone marrow and periodontal ligament derived-mesenchymal stem cells (Research Paper)

Mahshid Hodjat,[1,*] Mahdi Gholami,[2] Mohammad Sadegh Ahmad Akhoundi ,[3]

1. Dental Research Center, Dentistry Research Institute, Tehran University of Medical Sciences (TUMS), Tehran, Iran
2. Department of Toxicology and Pharmacology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
3. Dental Research Center, Dentistry Research Institute, Tehran University of Medical Sciences (TUMS), Tehran, Iran

Introduction: Diabetes Mellitus is an increasingly prevalent metabolic disease in the 21st century that is associated with long-term malfunction of different organs. Alteration of bone metabolism is the common complication of hyperglycemic exposure leading to an increased risk of osteoporosis-related fractures. Teeth surrounding alveolar bone could highly be affected by diabetes, undergoes gradual deterioration. In this project, we aimed to investigate the effect of epigenetic modifiers drugs on the osteogenic differentiation capacity of mesenchymal stem cell derived from diabetic rat bone marrow (BM) and tooth periodontal ligament tissue (PDL).

Methods: 8 wistar rats were included in the study and divided into two groups; Group-I: rats injected intraperitoneally with streptozotocin 60 mg/kg; Group-II: Control group injected with normal saline. The mandibles as well as femurs were dissected after three months. The cells were isolated and cultured from BM and PDL. The MSCs were characterized for surface markers using flow cytometry. The osteogenic capacity of MSCs-derived BM and PDL were assessed in the presence of epidrugs; Trichostatin-A (TSA) and Azacitidine (5-AZA) using Alizarin Red staining, ALP activity test and real-time PCR for gene expression analysis.

Results: The isolated cells were positive for CD105 and CD90 while there was low detectable cells with CD45+. The results showed reduced mineralization capacity of diabetic and normal rat BM and PDL MSCs in the presence of osteogenic medium containing high glucose. Adding Trichostatin A or 5-Azacytidine increased mineralization in MSC derived from diabetic rat BM and PDL. Adding TSA or 5-Aza also increased beta-catenin and GSK3ß the member of wnt signaling.

Conclusion: Hyperglycemic condition affects negatively the osteogenic potential of MSCs derived from bone marrow and periodontal ligament. Our results demonstrate that suppression of DNA methylation and histone

deacetylase could alleviate the impaired osteogenic differentiation capacity of diabetic MSCs. Our data indicate a role for the canonical Wnt signaling pathway in diabetogenic conditions. The data further implicated a role of epigenetic therapy in the treatment of osteogenesis complications of patients suffering from diabetic alveolar bone loss and diabetes-related bone diseases.

Keywords: Diabetes, Epidrugs, Bone marrow stem cell, Periodontal ligament stem cell, osteogenic differentiatio

The effect of bleeding stress during cesarean section in patients undergoing spinal: a review study (Review)

Mohammad amin Masoumi,[1,*] zeinab sadat moosavifard,[2]

1. BSc in Nursing, Department of Nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.
2. Department of Nursing, Faculty of nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.

Introduction: Cesarean section is one of the most common surgeries in the world. The rate of cesarean section in the world is equal to 15-20% and in Iran is equal to 40%. In cesarean section, 1000-750 cc is considered normal bleeding. Surgery is a stressful situation that triggers psychological and physiological reactions. A mother who goes to the operating room for a cesarean section is stressed because of the unfamiliar environment, the vague sounds of the monitor, the noise of other patients and operating room staff, the fear of the outcome or complications of the operation, and the anesthesia, the baby's health. Especially when spinal anesthesia is performed, because the patient is conscious and feels the surrounding stimuli during the operation, it is more stressful.

Methods: This review study was designed and performed to introduce and evaluate the effect of stress on bleeding during cesarean section. Materials and Methods: All data were obtained by referring to the authoritative scientific databases of Google Scolar, SID, Pubmed, Science Direct, Scopus and with the keywords Stress, Bleeding during surgery, Bleeding, Cesarean section, Spinal anesthesia. A systematic review was conducted in the period 2000-2009.

Results: In humans, one of the systems that responds to stress is the immune system. Under stress, increased cortisol decreases levels of proinflammatory cytokines and IL and α-TNF. Cortisol reduces immune cells at the wound site by stopping the proliferation and differentiation of immune cells, altering gene expression, and reducing cell adhesion. In cesarean sections, repair occurs in four stages: homeostasis, inflammation, proliferation, and tissue deformation. In the homeostasis stage, the immune system plays an important role in repair by producing pro-inflammatory cytokines. Stress can delay wound healing and prolong bleeding by reducing these cytokines. The majority of cesarean section patients undergo spinal anesthesia and are awake until the last moment due to special conditions and to prevent damage to the fetus, and they are not even injected with hypnotics. Therefore, these patients suffer a lot of stress. Researchers' clinical experiences show that patients with high stress tend to bleed more during a cesarean section.

Conclusion: Given that cesarean section is very stressful for the mother and can indirectly increase bleeding during cesarean section, so measures to reduce patients' stress seem necessary. Today, nurses use non-invasive, uncomplicated methods to minimize patient anxiety, including providing information about the patient's procedure, hand massage, aromatherapy, and music therapy.

Keywords: Stress, bleeding, cesarean section, spinal

The Effect of Boswellia Carteri Essential Oil on Morphology, Growth Kinetics and Differentiation of Bone Marrow-Derived Stem Cells (Research Paper)

Tahereh Emam,[1,*] Davood Mehrabani,[2]

1. Department of Biochemistry, Shiraz Branch, Islamic Azad University, Shiraz, Iran
2. Stem Cell Technology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

Introduction: Boswellia carteri (frankincense) is a gum resin of Burseraceae family with many therapeutic applications. Stem cells can differentiate into specialized cell and play an important role in treating a number of diseases. This study was undertaken to investigate the effect of Boswellia Carteri on morphology, growth kinetics and differentiation of bone marrow stem cells (BMSCs).

Methods: BMSCs were provided from femoral bone of Guinea pigs and were seeded in a 24-well plate. They were characterized morphologically and for osteogenic differentiation property and by RT-PCR for mesenchymal marker CD90 and hematopoietic marker CD34. BMSCs at passage 4th were exposed to different doses of essential oils of B. carteri. Cells were collected from each well 1–8 days after seeding and population doubling time and cell growth curves were determined.

Results: BMSCs were all adhered to the culture flasks and displayed spindle-shape morphology. An increasing growth and mitotic division were shown for all doses of frankincense. All cells were positive for mesenchymal marker and osteogenic induction after exposure to frankincense. From day 5th to 8th, cell growth in all three groups of exposure to B. carteri was significantly higher than the control group.

Conclusion: Conclusion: The findings of this study revealed that Boswellia carteri (frankincense) has an increasing and positive role in the growth of bone marrow mesenchymal stem cells and these results can open a new window in the laboratory and clinical research of stem cells.

Keywords: Boswellia carteri, Growth, Mesenchymal stem cells, Bone marrow

The effect of caffeic acid phenethyl ester on Interleukin 10 (IL-10) and Interleukin 33 (IL-33) anti-inflammatory cytokine expression in Wistar rat model with Alzheimer's disease (Research Paper)

Fatameh Rouhollah,[1,*] Maryam saeidi,[2] Shadi Jafari,[3] Esmaeil Emdadi Siyah Pirani,[4] Seyed Hamid Jamaloddini,[5]

1. Department of Molecular and Cellular Biology, Faculty of Advanced Science and Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran
2. Tehran Medical Sciences, Islamic Azad University, Tehran, Iran
3. Department of Molecular and Cellular Biology, Faculty of Advanced Science and Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.
4. Department of Molecular and Cellular Biology, Faculty of Advanced Science and Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran
5. Department of Genetics, Faculty of Advanced Science and Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

Introduction: Alzheimer disease is one of the brain functional disorder, which influenced on memorize and mental ability of patients, slowly. Interleukin-10 acts as an immune regulator in inflammatory situation. Also Interleukin 33 (IL-33) is a cytokine belonging to the IL-1 superfamily. IL-33 induces helper T cells, mast cells, eosinophils and basophils to produce type 2 cytokines. The Caffeic acid (3, 4- dihydroxy cinnamic acid) is one of the most importance of hydroxycinnamic acid in Propolis that its antioxidant effect could block NF-kappa B pathway

Methods: The present study was performed on wistar rat, these animals were divided into 6 groups (control, sham, scopolamine, 1, 3 and 8 Caffeic acid phenethyl ester recipients). The DNA was extracted from their brain tissue. Then IL-10 and IL 33 genes expression was evaluated by QRT-PCR. The histopathological examinations were performed on brain sections

Results: The number of remaining healthy neurons in the Caffeic acid phenethyl ester treated group 3 mg was more than the number of these cells in the treatment group with Caffeic acid phenethyl ester 1 mg. Although the highest number of normal cells were observed in sham group and treated with Caffeic acid phenethyl ester 8 mg. The molecular studies also showed that the expression level of IL-10 and IL-33 genes were significantly increased in the group treated with 3 mg drug.

Conclusion: Using an effective dose of Caffeic acid phenethyl ester, as an anti-inflammatory compound, can improve Alzheimer through impact on the IL-10 and IL-33 genes expression and the memory and learning improvement and reducing cellular damage. However, more extensive studies are still needed in this area

Keywords: Alzheimer, Caffeic acid phenethyl ester, Interleukin 10, Interleukin 33, wistar rat

The effect of carbamazepine in the treatment of Alzheimer's (Research Paper)

Ali Khanifar,[1,*]

1. Kurdistan university of medical sciences

Introduction: As you know, in Alzheimer's disease, two complications are most prominent, one is amyloid plaques and the other is hippocampal analysis. A US university study of amyloid plaques found plaques in people with dementia, but surprisingly, people with no history of dementia had amyloid plaques.According to this study, it can be concluded that amyloid plaques are an accelerating factor in Alzheimer's disease but not a 100% factor. In this research, a new method is used in the treatment of Alzheimer's, which will also use seizure drugs, especially carbamazepine, as a treatment for Alzheimer's. In Alzheimer's disease, neurons connected to the hippocampus become contracted and lose their connection to the hippocampus, causing the hippocampus to begin to degenerate over time. Among the drugs used to treat seizures, carbamazepine causes a strong memory in people who use it for a limited time, and when they stop taking it, they experience a kind of memory loss.

Methods: Carbamazepine is a sodium channel blocker. In fact, this action causes the humidity of the brain waves between all parts of the brain, which takes the neurons out of the curved state in all parts of the brain and returns them to their part, and prevents the failure of the desired part, especially the hippocampus.To prove this theory, two mice are needed in the laboratory, one young and the other 5 years old, which is equivalent to an old human. First, we put the young mouse in a tortuous corridor and we see that the young mouse leaves this corridor with 2 routing times, but another mouse, which is the same age as an old human, leaves the ability to leave after 6 to 7 routing times. It has this corridor, but by injecting carbamazepine into old mice, I see that over time, the old mouse's ability to get out of the corridor gets better and better.

Results: In fact, taking carbamazepine by Alzheimer's patients will prevent hippocampal resorption, and this is done by reversing neurons. Because brain cells, especially the hippocampus, will not be able to repair, treatment with carbamazepine should be started as soon as possible.

Conclusion: As mentioned, this drug is used to treat seizures that, due to the balance and humility that it shows in different parts of the brain, prevents the breakdown of the hippocampus, which plays a key role in Alzheimer's

disease.The drug also boosts memory in some patients and interrupts memory loss.

Keywords: Carbamazepine - Alzheimer-Amyloid plaques -Hippocampal - Memory loss

The effect of computer cognition games on communication skills and emotion regulation in children with autism disorder (Research Paper)

Iman Mosalanezhad,[1,*] zeinab sadat moosavifard,[2]

1. Master of Educational Sciences. Education of Fars province, Iran.
2. Department of Nursing, faculty of nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.

Introduction: For most children without disabilities, a desirable and cohesive pattern of social relationships with peers is naturally created. However, children with neurological disorders are at risk for having problems with peers. This is especially true for children with autism; Because, according to the American Psychiatric Association, social and communication disorders are a hallmark of children with autism. Through play, social barriers can be reduced to smaller challenges because play facilitates social interactions not only through conversation but also through rewarding activities. Play also contributes to the development of autonomy, identity and self-control in these children. Computer games have a different effect on children's problem-solving abilities and skills. The aim of this study was to investigate the effect of computer cognitive games on communication skills and emotion regulation in children with autism spectrum disorder.

Methods: For this purpose, during a quasi-experimental study with pre-test-post-test and control group, 44 children from 8 to 11 years old with autism were selected by available sampling from rehabilitation centers in Shiraz and used in two experimental and control groups. Were. Groups were assessed before and after the intervention with the SCQ Social Communication Questionnaire (Rutter, Bailey, & Lord, 2003) and the Emotion Regulation Questionnaire (Shield and Kicketti, 1998). The experimental group was trained in computer cognitive games in 12 sessions of 45 minutes and 3 sessions per week.

Results: The results of analysis of covariance showed that computer cognitive play had a significant effect on emotion regulation in children with autism, but this effect was not significant on communication skills. The results of this study showed that the use of computer cognitive games was effective on emotion regulation in children with autism spectrum disorder.

Conclusion: Play has a great impact on the child's personality and development. In the form of play, the child perceives countless patterns in the complex and delicate life, experiences and practices it, and measures the relationship between the patterns in order to learn them. Because it has to face them in adulthood and also plays an important role in language learning.

In general, play is very effective in the development of the child's intelligence. We need to know that play is a platform for children with autism to climb. Playing for children is like talking to an adult, games and toys are children's words.

Keywords: Computer cognitive play, emotion regulation, communication skills, and autism spectrum disorder

The effect of couple based motivational interview in pregnancy on men's smoking at home (Research Paper)

Roghieh Bayrami,[1] Samira Ebrahimi,[2,*]

1. 0000-0001-7122-8035
2. 0000-0003-1306-7741

Introduction: Background and Aim: Complications of exposure to second-hand smoke (SHS) are known to affect the health of pregnant women and fetus. It requires designing an intervention to reduce the exposure of pregnant women to smoke. This study, therefore, aimed to examine the effect of couples motivational interview in pregnancy on men's smoking at home.

Methods: The present study is a clinical trial study. 112 couples (56 non-smoking pregnant women with smoking spouse) were enrolled in the study. Sampling was performed in several steps. First, according to the social, economic and cultural conditions of the city, Urmia was divided into three sections, and two comprehensive health centers were randomly selected from each section. Blocked randomization method was used for random allocation in control and intervention groups. The motivational interview was conducted in 5 sessions of 60 minutes twice a week for intervention group. The control group received routine prenatal care. Post-test was performed in the control and intervention groups 7 days and 30 days after the intervention. Data were analyzed using a repeated-measures analysis of variance by SPSS-20 at a significance level of 0.05.

Results: The median number of cigarette smoked ,before intervention, one week, and one month after the intervention were (70-172/5) 110 , (40-135/5) 70 and (46-122/5)69.50 respectively. The results showed that these decreasing changes were statistically significant (P <0.001).

Conclusion: Couples' motivational interview can be used to reduce smoking by the spouse, which ultimately changes the behavior of the pregnant women to reduce exposure to secondhand smoke.

Keywords: second hand smoke, pregnancy, motivational interview

The Effect of COVID _19 on Menstruation (Review)

Mehrdad Ostadpoor,[1,*] Ahmad Zeinodini,[2] Seyyed Hossein Heidari,[3] Pooria Rezaei,[4]

1. Graduatedof Veterinary Medicine Faculty, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran
2. Graduatedof Veterinary Medicine Faculty, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran
3. Graduatedof Veterinary Medicine Faculty, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran
4. Graduatedof Veterinary Medicine Faculty, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran

Introduction: A pathogen from a human-animal virus family, the coronavirus (CoV), which was identified as the main cause of respiratory tract infections, evolved in to a novel and wild one in Wuhan (a city in Hubei Province of China) and spread rapidly throughout the world, so it created a pandemic crisis according to the World Health Organization. these viruses cause different diseases such as common colds in human and animal. they sometimes attack the respiratory system or their signs appear in the gastrointestinal tract. in the world, people experienced physical stress, virus infection, related complications, mental stress and panic caused by the public health emergency. the most common symptoms of COVID_19 which appear in patients who were infected to COVID _19 include cough, fever, even respiratory failure, dyspnoea, myalgia, headache, diarrhoea, rhinorrhoea, a sore throat. pharyngalgia, sudden gustatory and olfactory dysfunctions were also other important symptoms in patients infected by COVID _19.

Methods: In the current study, key words including COVID_19, Coronavirus, Menstruation and Stress were reviewed from the list of Mesh and other credible websites including PubMed, Science Direct ,Google Scholar and the data were organized.

Results: Result indicate that although no obvious menstrual cycle change was observed, women who affected by COVID_19 have a significantly lower serum anti-mullerian hormone level and higher testosterone / prolactin level, suggesting a poor ovarian reserve and abnormal reproductive hormones compared to the age-matched healthy unaffected women. some researchers say anxiety levels were high in participants during the COVID_19 pandemic. it was seen that the stress levels of women during the pandemic have increased due to psychiatric impacts. almost half of the women reported that they had periods which were heavy and painful that shows a significant increase compared to their periods before the pandemic. While a significant proportion of women described the negative impact of the pandemic on their

menstrual cycle and lifestyle, there was a minority of women who described some positive effects. some women noted they had more regular periods and periods which were less heavy and painful and they had less premenstrual symptoms. some women reported increase level of libido in themselves. some women described positive aspects of the pandemic; including a slower pace of life, less commuting and spending much more time with their families. some women recognised both a positive and negative impact of the pandemic on their lives. it is still impossible to know if the pandemic continues and progress any positive effects will endure.

Conclusion: Increased levels of anxiety and stress due to the prevalence of COVID _19 have a significant effect on women's menstrual cycle however we need more studies to get better conclusion.

Keywords: COVID_19, Coronavirus, Menstruation, Stress

The effect of curcumin on lung csf secretion and evaluation of its antioxidant enzyme activity (Research Paper)

saba zakeri,[1,*] Zahra Zamani ,[2] Sahel zakeri ,[3] Zahra Mehdipour ,[4] Karim Zamanfar ,[5]

1. Phd student of Clinical Biochemistry, kermanshah University of Medical Sciences, Kermanshah, Iran
2. 1. Department of Biology, Faculty of Basic Sciences, Science and Research Branch, Islamic Azad University, Tehran, Iran.
3. Department of Biology, , Faculty of Basic Sciences, Islamic Azad University,Sanandaj,Iran
4. Department of Biology, , Faculty of Basic Sciences, Islamic Azad University, Karaj, Iran.
5. Department of Medical sciences, Clinical Research Development Unit of Imam Reza Hospital, affiliated to Kermanshah University of Medical Sciences, Kermanshah ,Iran

Introduction: Curcumin, a yellow pigment from Curcuma longa, is a major component of turmeric and is commonly used as a spice and food-coloring material. It exhibits anti-inflammatory, antitumor, and antioxidant properties., Colony-stimulating factors (CSFs) are secreted glycoproteins that bind to receptor proteins on the surfaces of hemopoietic stem cells, thereby activating intracellular signaling pathways that can cause the cells to proliferate and differentiate into a specific kind of blood cell. Numerous studies have shown the antioxidant role of colony stimulating factor .The aim of the present study was Investigation of the Effects of two types of curcumin monomer and polymer on lung csf secretion through bone marrow cell colonization and evaluation of its antioxidant activity in Balb mice in Balb / C mice.

Methods: In this study, we used Balb / C mice, which is one of the most suitable breeds for bone marrow culture. Bone marrow cells were obtained as a source of hematopoietic stem cells from the femur and tibia of mice. Mice lungs were also cultured as CSFs secreted tissue to prepare CSFs.

Results: Each experiment was repeated three times. Mean and standard deviation from the results were determined. SPSS test was performed by ANOVA method at the level of $p < 0.05$ and the comparison between the results was significant. In the presence of curcumin monomer and curcumin polymer, the antioxidant enzymes, catalase, superoxide dismutase, glutathione peroxidase activity at certain concentrations increased , This increase is statistically significant for $P < 0.05$ compared to the control and then fall down at more than this concentration.The results of this study are consistent with previous studies in which the effects of curcumin on antioxidant activity have been investigated.

Conclusion: in concentrations 30 µg/ml polymer curcumin and 25µg/ml monomer curcumin significantly secretion of CSF and the activity of the antioxidant enzymes catalase, superoxide dismutase, glutathione peroxidase increases And in higher concentrations have the opposite effect.

Keywords: antioxidant enzymes, curcumin, Colony-stimulating factor, lung tissue,mice, bone marrow cell

The effect of dental pulp mesenchymal cell function on tooth growth and restoration (Review)

zakiyeh khosravi,[1,*]

1. Forough Danesh Sample School

Introduction: Mesenchymal cells of the teeth, including mesenchymal cells of the third molars, are a very rich source of dental pulp cells that after collection, culture and passage can be found in special laboratory conditions that these cells are located in all individuals (adults, children and even fetuses). They have the possibility of using these cells in any period without any restrictions. The hidden point that can be found in the use of these cells is the optimal function of these cells in medical science, because of all the harms and problems that can be predicted in implants and ... It is far.

Methods: Survey in people 18-25 years old Fourteen specimens were collected from the pulp and six specimens from the third molar's dental follicles in adults between the ages of 18 and 25 years. These teeth had no previous caries or restoration, and all patients were healthy and had no systemic disease. They were taken and transferred to the Molecular Cell Laboratory at 4 ° C. To reveal the pulp chamber of the teeth, they were cut from the enamel-cement joint with a carbide disk and a handpiece, and thenThe pulp was separated from the pulp chamber by a fine file of the pulp; Then, for cell culture of pulp and follicle tissue, these cells were divided into smaller pieces by surgical blade No. 10, and then they were placed in Falcon containing 4 mg / ml of collagen type solution (sigma I), 104 mg / ml. Gibco type dipase solution with a ratio of 1/1 was exposed to 37 ° C for 45 minutes and then added to the lysed tissue of the culture medium and centrifuged at 600 g for 10 minutes. Mixed cultures were transferred to a suitable zvt in an incubator at 37 ° C, 5 atmospheres and 2% CO2. This culture medium was changed every two days until 70% of the plate bottom was filled with cells when the plate bottom reached 70% filling. Were passed using trypsin _EDTA Finally, flow cytometric analysis was used to evaluate the phenotypic profile of surface markers and the nature of stem cells from the pulp and follicular tissue of the third molar. With a concentration of 1,000,000. The cells were then divided into 6 tubes and PE 5µl was added to each tube with antibodies. The tubes were then placed in a dark environment at 4 ° C for 30 minutes, after which time the cells were washed with 1 ml of wash buffer. They were centrifuged at 1200 MPR for 5 minutes, after which each cell sample was suspended in 300 l to 500 l of washing buffer and analyzed by flow cytometry. The second experiment in children In this experiment, the pulp of children's deciduous teeth that were extracted for dental reasons was used. After removing the teeth and collecting them and transferring them to the laboratory environment, the teeth were first rinsed with distilled water and phosphate

buffer solution. They were made of polymer and can be ironed, where the teeth were centrifuged and the surface of the Falcon was discarded. The teeth were then removed from the falcons and rinsed thoroughly with distilled water. It was pink and very thin. It was cut into several pieces by the surgical file inside the culture medium. Because the cell separation process was very time consuming, two separate methods were used to accelerate the cell separation process: 1) Crushed particles with trypsin and collagen {, both of which are considered body lubricants and have a powdery structure and must be dissolved to add to the composition. These two substances must be refrigerated to be always active, and if They are out of the refrigerator for more than half an hour and lose their lubricating properties. They entered the Falcon. The Falcon containing pulp and trypsin tissue was placed in the refrigerator for 8 hours. Falcon contents slipped into a small flask under the hood. 2) In another falcon, the pulp was placed directly in the refrigerator without adding trypsin and collagen. The test was performed and after emptying the contents of the falcon, it entered the incubator in small flakes. 90 ° C and 2% carbon dioxide and 32% humidity were stored for a period of time until the cells separated. The flakes were placed under an inverted microscope once a day and the condition of the tissues was examined. When the first cell lines were separated from the tissue, the cells were transferred to a 2 ml flask by passage. These cells were called HDPCs and after expiration About 6 months after the separation of pulp tissue inside each bifurcation, the first cell lines were observed. These cells were completely elongated and had a needle-shaped appearance. After filling the bottom of the dish, cell passage was performed with trypsin and finally, depending on the number Cells from each cell passage sample were taken.For the next period, the cells were used in the fourth passage in an environment containing 27 DMSO and 47%. Mesenchymal stem cells were transferred to a nitrogen tankThey were then differentiated into fat and bone using differentiated culture media to prove that these cells were stem cells.

Results: According to the mentioned cases, it can be said that in adult cells in adults, there are also mesenchymal stem cells of dental pulp, because after a dental injury, dentin is repaired by making and depositing dentin matrix to repair the damaged area. This restorative process takes place throughout a person's life, which indicates the presence of mesenchymal cells in the pulp of adult teeth and the ability to make odontoblasts under the influence of appropriate signals.But the whole potential of adult stem cells is not as great as that of embryonic and childhood stem cells(Which is extracted from the gums, especially from the posterior gums) or the use of mesenchymal stem cells in deciduous teeth. These cells, as mentioned, are not limited to any age group and even the ability to donate these cells from one person to another is possible. Is acceptable and the condition for donating teeth: The complete health of the person and the donor's teeth, which can be done even in adulthood when most people have lost their deciduous teeth (except occult

deciduous teeth) from the mesenchymal stem cell gene of children or fetuses to repair and restore teeth. In the laboratory method, mesenchymal stem cells in adults, although they can be repaired or regenerated, but after they are separated from the patient, they must first go to the laboratory and after strengthening and differentiating them, they are injected into another person as a plum or xenophore recipientHowever, due to the many problems that occur during amplification, injection, long time and less potential and compatibility of these cells, problems such as premature tooth decay, tooth loss, immune system attack on these cells through the immune response, etc. may occur. In this regard, it can be said that the use of secondary methods (experiments: laboratory culture of cells, mesenchymal cells of deciduous teeth) have more function and efficiency in this field. And given the problematic factors that exist in adult mesenchymal cells, the protocol for this ideal for humans is relatively far from being applicable. In dental restorations, it can be reported that a shorter course of treatment in dental restorations using stem cells has taken place (because in the two experiments mentioned above, restorations and restorations of teeth have taken a relatively long period). By activating stem cells, these cells can send messages to stem cells that greatly help activate repair and amplification cells (this is also possible with low-power lasers), resulting in the formation of dentin cells.(Hard tooth tissue) helps a lot.

Conclusion: So it can be said that tooth regrowth is a fact, not an ideal, and given that the tooth is made up of two different types of tissue, logically making a tooth requires communication and cooperation with epithelial cells and odontogenic mesenchyme. Recombinant epithelial tissue and dental mesenchyme to form teeth in both the laboratory and the living environment allow the combined cells to organize and form individual layers and also to be able to differentiate odontoblasts and amyloblasts. In order to make a complete tooth that also has enamel and dentin, epithelial and mesenchymal cells are inserted into the collagen gel solution, respectively, and then implanted inside the oral cavity, and with this technique, the presence of all dental structures such as odontoblasts, amyloilasts, pulp, Blood vessels, crown, root, periodontal ligament and alveolar bone are observed, so implantation of this dental mass (mesenchymal + epithelial cells) leads to the development of puberty and regrowth of teeth. Therefore, it can be said that using modern engineering and methods, mesenchymal stem cells extracted from tooth pulp and deciduous teeth can be used to repair tooth tissues under tissues that have mesenchyme and connective tissue infrastructure. Any age is able to regrow its teeth using the mesenchymal stem cell gene and it is worth noting that the use of mesenchymal gene is not limited from one person to another(No age limit for people) and another point is that the use of this method if the mesenchymal gene used is healthy unlike implants has no restrictions and no harm and replacement of this Methods Instead of modern methods, dentists can use it more economically and efficiently.

Keywords: Mesenchymal stem cells_tooth pulp _tooth follicle

The effect of diabetes disease on the expression of INSR & IRS-1 genes in infertile women (Research Paper)

Nader Namvarsigaroudi,[1] Zahra TahmasebiFard,[2,*]

1. Department of Biology, Roudehen Branch, Islamic Azad University, Roudehen, Iran
2. Department of Biology, Roudehen Branch, Islamic Azad University, Roudehen, Iran

Introduction: Introduction: Infertility is a disease with complex disorders that occurs for a variety of reasons, some of which remain unknown. Infertility factors include a wide range of hormonal, immunological, physiological, weight, and physical activity factors. Genetic factors play a key role in reducing fertility. Balance of insulin hormone affects other important body hormones such as estrogen; progesterone and testosterone imbalances in these hormones have a wide range of side effects, including endometrial tissue and infertility. Objective: The purpose of this study was to investigate the expression changes of insulin receptor genes (INSR) and insulin receptor substrate (IRS-1) in the pathway of insulin signaling to endometrial tissue of infertile women compared between diabetic and Healthy women.

Methods: Materials and Methods: In this study, thirty infertile women (4 diabetics, 26 healthy) who had been married for more than five years, an unknown cause of infertility, regular menstrual cycles, normal ovarian function, and absence of abnormalities in the uterus and fallopian tubes, or signs of endometriosis on ultra-sonographic or laparoscopic examinations were selected; in addition, the spouses of these people had normal volume and analysis of semen according to WHO criteria. Those who did not have this characteristic were excluded. Endometrial tissue of all women was prepared to evaluate the expression of INSR & IRS-1 genes using the Real-Time PCR method after RNA extraction.

Results: The results of this study showed that the parameters (Age & BMI) induced different changes in INSR and IRS-1 gene expression in both infertile subgroups and were statistically different. The Comparison of INSR & IRS-1 genes expression levels in endometrial tissue of healthy and diabetic individuals in each group showed a decreasing gene expression in the diabetic infertile woman and a significant difference between them. Healthy infertile persons showed 21.35 times more expression of the INSR gene than infertile persons with diabetes and 16.82 times more expression for the IRS-1 gene.

Conclusion: Diabetes affected the expression of genes and caused a reduction in the expression of both genes in persons with diabetes compared to healthy persons. His data can be one of the effective reasons for unspecified abortion. These genes are probability strong molecular markers for infertility.

Keywords: Female infertility, Insulin Receptor (INSR), insulin receptor substrates -1(IRS-1), abortion

The effect of different size reduction methods on the doxycycline-containing niosomes, prepared for the skin infection treatments (Research Paper)

Fatemeh Kashani-Asadi-Jafari ,[1,*] Afra Hadjizadeh ,[2]

1. Amir Kabir University of Technology
2. Amir Kabir University of Technology

Introduction: Dermal drug delivery to treat skin infections uses drugs topically, and is superior to oral drug delivery. This delivery method reduces systemic absorption and reduces the hepatic metabolism of the drugs. It also has a fixed and controlled drug input source that can prevent the changes of drug levels in the plasma. The most crucial barrier to dermal delivery is the stratum corneum, which acts as a barrier to drug penetration. Topical use of conventional drug formulations causes side effects and a lack of targeted drug delivery. Therefore, nanocarriers are used for topical drug delivery to overcome the obstacles to the targeted dermal layer. One of the nanocarriers is niosomes. In this study, a niosomal formulation containing doxycycline, the safest and most influential of tetracycline antibiotics, with a molar ratio of 8: 2 span 60/cholesterol was prepared and characterized

Methods: Niosomal formulation preparation method The thin-film hydration method was used for niosomal formulation. First, the appropriate values of span60 and cholesterol with an 8:2 molar ratio and the total lipid of 700µmol were dissolved in 15 ml of chloroform and then transferred to a rotary evaporator at 60°C and 120rpm under reduced pressure. After chloroform evaporation, the thin film inside the balloon was hydrated by the drug solution at at 80rpm and 60°C (10µmol of doxycycline in 15ml PBS (pH=7.4)) under normal pressure for 60 minutes. Size reduction methods Three methods were used: Bath sonicator: 5ml of suspension was sonicated for 45 minutes. Extrusion: 5ml of suspension was passed five times through a polycarbonate membrane with a porosity size of 200nm. Probe sonicator: 5ml of suspension was sonicated for 15 minutes at 150watts (8 seconds on and 2 seconds off). Characterization Particle The morphology of the prepared sample was observed using the Scanning electron microscopy (SEM) after each size reduction method. Particle size Diameter size was measured with a dynamic light scattering analyzer(DLS). Entrapment efficiency and drug loading capacity 10ml of suspension was centrifuged via ultracentrifuge at 30,000rpm (100,000 × g) at 25°C for 15 minutes. The supernatant containing the free drug was separated from the pellet. Then its absorption at 276nm was measured with a spectrophotometer. Furthermore, the desired parameters were obtained using the following equations: "EE%" "=" "(the initial amount of doxycycline - the amount of doxycycline in the supernatant)" /"the initial amount of doxycycline" "×100" "LC% = " "(weight of initial doxycycline-weight

of free doxycycline)" /"weight of nano-niosomes" "×100" Drug release The synthesized formulation and free-drug (with the equivalent drug) were transferred to a dialysis bag (12,400Mv cut-off) in a beaker with a content of 20 ml PBS (at 37°C and a vortex of 100rpm). 1ml sample was taken from the inside beaker at 0.25, 0.5, 1, 2, 4, 8, 16, and 32hours. The absorbance was measured at 276nm. Finally, drug release data were analyzed using Zero-order, Higuchi, and Korsmeyer-Peppas kinetic models.

Results: SEM:The bathing method had almost no effect on reducing the sample size. The inefficiency of the extrusion method was also observed. Span60 is solid at room temperature, and extrusion must be performed at temperatures above Tc of surfactant because it has a low velocity at temperatures below Tc due to the higher gel viscosity of the membrane and reduced ductility. The extrusion method also changed the morphology of the niosomes, which may be due to the low percentage of cholesterol in the sample structure, which loses its flexibility when exposed to high force. Therefore, size reduction with the probe sonicator is the best way to reduce sample size. Particle size: The DLS results showed an average particle size of 213.76±12.75nm. The entrapment and loading capacity of the drug: The obtained values were 39.7±1.8 and 13.4±0.6, respectively. Drug release: Controlled and slow drug release from the prepared formulation compared to the free-drug was observed after 32 hours. The most consistent release data were with the Korsmeyer-Pappas model ("R" ^"2" " ≥ 97%").

Conclusion: The sample synthesized by the thin-film hydration method and probe sonication had a suitable size for dermal delivery, and the drug entrapment efficiency was appropriate. In addition, controlled release of the drug prevents skin side effects compared to the free drug and reduces the need for re-dosing. Thus, in general, the synthesized sample can be used in dermal delivery and skin infections

Keywords: Nanoniosome, Doxycycline-hyclate, skin.

The Effect of eNOS Gene Expression On Diabetes-Related Depression In Patients With Type 2 Diabetes (Research Paper)

Mahsa Khosrogardi,[1,*]

1. Payame Noor University . Tehran , Iran

Introduction: Diabetes is a chronic metabolic disease and a major health problem that is on the rise, especially in developing countries. Overall, the number of patients with diabetes in the world is more than 250 million and is projected to increase by 350 million in 2020 and more than 438 million in 2030. The chronic nature of diabetes has a great impact on the patient's body-mind and individual and social functioning, and therefore the study of various aspects of health in these patients is of particular importance. (Mirsifi et al., 2018). As mentioned, chronic diabetes occurs when the body is unable to produce enough insulin or to use insulin effectively, which can be due to genetic factors and environmental factors. (Harris and Zimmet, 1997). In 2011, there were 366 million people with diabetes worldwide, half of whom are still unaware of their disease. It is also predicted that by 2030 the number of people with diabetes worldwide will reach 552 million. The prevalence of type 2 diabetes is becoming a major problem for human health because the figures for the statistics provided in the coming decade are doubling, and as a result, diabetes in adults will become a problem. Weight gain, sedentary lifestyle, and diet are some of the factors that contribute to type 2 diabetes. (Sally et al., 2004). Type 2 diabetes (T2DM) is the most common form of diabetes and causes impairment in insulin secretion and insulin resistance (Deferonzo et al., 2007). As mentioned above, chronic diabetes occurs when the body is unable to produce enough insulin or use insulin effectively, which can be due to genetic backgrounds and environmental factors. In 2011, around the world, 366 million people had diabetes, half of whom are not yet aware of their disease. It is also predicted that by 2030 the number of people with diabetes worldwide will reach 552 million. The prevalence of type 2 diabetes is becoming a major problem facing human health as the amounts of statistics presented in the decade ahead are doubling, resulting in diabetes in adults becoming a problem. Weight gain, the prevalence of living, and low-stimulation life, and diet are among the factors in the incidence of type 2 diabetes. The prevalence of this patient in European countries is 7% of the total population, which is 5-7% of the total population in the world. This estimate cannot be so real because in many cases it can be said that 50% of people with diabetes are unknown. Studies show that the rate of diabetes in urban areas is higher than in rural areas. The overall goal in managing type 2 diabetes is to control blood glucose and reduce the risk of long-term complications. Numerous studies have shown that modern management can limit, delay, and even prevent the long-term effects of diabetes by tightly controlling blood sugar levels. Managing blood sugar in type 2 diabetes has

become a complex and somewhat controversial process because different drugs have been suggested to do so, but the increase in available drugs has also raised concerns in this regard because these drugs always have side effects. They are associated with the fact that controlling and managing blood sugar levels is necessary and has many benefits in preventing cardiovascular disease. As mentioned, people with type 2 diabetes are at higher risk for cardiovascular disease, which increases mortality in people with diabetes (Nenoi et al., 2011). Depression is one of the most common psychiatric disorders that leads to significant complications for the active stratum of society, which can significantly reduce patient performance in all areas of occupation, social, and family relationships. Half of the patients with depression are in the age range of 25 to 65 years and epidemiological findings indicate an increase in the prevalence of depression in under 20 years of age. Depression is a disorder in the presence of a depressed mood for at least two weeks, which is usually associated with decreased concentration, difficulty in decision-making and irritability or psychomotor slowness, guilt, and thoughts related to death. Various factors have a role in the development of depression, including biological factors such as serotonin nervous systems, norepinephrine, dopamine, genetics, psychosocial factors such as various life events, and recently various internal stressors such as changes in serum cholesterol levels, triglycerides, sugar and coagulation factors are involved in depression. Depression, in addition to causing physical problems and exacerbating some symptoms such as pain, affects and reduces the ability and function of the individual. Also, the power of decision-making is stripped and the ability to take care of oneself is lowered, resulting in the independence of the individual and creates dependence, disability, and lack of self-confidence (Mirsifi Fard and others, 2018). Changes in the interactions of neurotransmitters in the serotonergic, dopaminergic, and adrenergic nerve pathways manifest themselves in the form of depressive symptoms. According to the above, this study was performed to investigate the effect of eNOS gene expression on diabetes-related depression in patients with type 2 diabetes referred to Shariati Hospital - Endocrinology and Metabolism Research Institute of Tehran University of Medical Sciences.

Methods: This study is of case-control type. The participants of this study are those who were referred to the diabetes clinic of Dr. Shariati Hospital. A demographic and clinical information registration questionnaire was completed for each candidate with the cooperation of the treating physician. The case group includes (50) people with type 2 diabetes and depression and the control group includes (50) people with type 2 diabetes and no depression. People with type 2 diabetes will have people with a fasting blood sugar of 6 126 mg/dl, which was confirmed during repeated tests, and people with diabetes will have no complications of diabetes such as retinopathy, neuropathy, and nephropathy. Confirmation of depression will be done with the opinion of the treating physician. After completing the questionnaire and

consent form, the participants in the study were sampled in tubes containing EDTA. After sampling, RNA extraction was performed using the TRIzol method and qualitative analysis of RNA extracted by gel electrophoresis and also quantitative analysis of RNA extracted by nanodrop device. GAPDH and eNOS primers were then designed. Then, PCR reaction and cDNA synthesis were performed to amplify the desired fragments, and finally, real-time PCR was performed to evaluate the expression of the desired gene. SPSS software was used for data analysis. A P-value less than 0.05 was considered statistically significant. Specifications of Designed Primers Table 1 shows the characteristics of primers designed to evaluate the effect of eNOS gene expression on diabetes-related depression in patients with type 2 diabetes (Abbaszadeh Goodarzi, 2015). The primer was designed by experts from the Endocrine and Metabolism Research Institute of Shariati Hospital. For Real-Time PCR of 10 l volume (cDNA), 5 µl was removed (not diluted) and stored at -80 ° C after the ThermoCycler was completed. DEPC was added to the remaining 5 µl of water and a total of 20 µl was used for Real-Time PCR. The Real-Time PCR used in the Endocrinology and Metabolism Research Institute is a model (LightCycler ® 96 for Roche). In this study, eNOS specific primer was used and GAPDH primer was used as a positive control for cDNA synthesis. Real-time PCR was used to compare the pattern and expression of the eNOS gene between the two groups (patients with type 2 diabetes with depression and without depression). In this method, after preparation and extraction of RNA and cDNA synthesis using Reverse primer and cDNA synthesis, a complementary DNA strand was made and samples obtained at a concentration of 500 ng / µl were used as a model for Real-Time PCR. The reaction was performed using SYBER Green PCR. How to combine the materials to make the reaction mixture was done according to the table below (Table 2).

Results: Quantitative Results Of RNA Extraction From Blood Using A Nanodrop Device To evaluate the purity of the extracted RNAs, the absorption ratio at 260 and 280 nm was used by the nanodrop device and minimal protein contamination was used. In Table 4, the quantitative results of RNA extraction of several samples can be seen. Qualitative Results Of RNA Extraction From Blood Using Electrophoresis In addition to quantitative results, gel samples were taken to ensure the presence of RNA and the absence of DNA contamination. After viewing the images, the accuracy of the work was ensured. Results of cDNA synthesis using GAPDH (Housekeeping Gene) primer After ensuring the quality of the extracted RNA, a complementary DNA strand (cDNA) was made from the samples using the reverse transcriptase (RT) enzyme. The quality of cDNA was evaluated by RT-PCR technique and using GAPDH primer to ensure the presence of cDNA and DNA contamination. The results are shown in Figure 2. Check the result of Real-Time PCR Evaluation and comparison of eNOS gene expression in patients with Real-Time PCR technique The present study was performed to

evaluate the expression of nitric oxide synthase gene in type 2 diabetic patients with depression and non-depressive type 2 diabetic patients. The result of eNOS gene expression by Real-Time PCR showed that in patients with type 2 diabetes with depression compared to patients with type 2 diabetes without depression, the expression of this enzyme gene was increased which is not statistically significant (p> 0/05) (Figure 3) Statistical analysis results The results of eNOS gene expression are shown in Figure 4-a. As the expression of the eNOS gene has increased in the case group compared to the control group, this increase is not statistically significant (p> 0.05). Also, in the histogram of Figure 4-b, it can be seen that the expression of nitric oxide synthase gene has increased in the case group compared to the control group, which is not statistically significant (p> 0.05).

Conclusion: Multiple studies show that depression is more common in patients with type 1 and type 2 diabetes than in healthy people. Worldwide, depression in diabetics is linked to the culture or society of countries. It is reported that 26% of patients with diabetes worldwide have depression. In these patients, the level of quality of life has decreased so much that the resulting mortality is increasing (Aswar et al., 2017). Diabetes mellitus such as body mass index (BMI), family history of diabetes, smoking , physical activity, diet, and alcohol consumption remain significant. Also, in depressed diabetic patients, blood sugar control is more difficult, and diabetic complications are more. In Iran, many studies have been conducted to investigate the prevalence of depression in diabetic patients and the presented statistics are reported to be between 11-91% different. Therefore, a structured review of all documents and their combination can lead to a more complete picture of the dimensions of this problem in Iranian society (Azami et al., 2017). According to various studies, 15-32.5% of diabetics suffer from depression. The lifespan of people with diabetes is clearly higher than that of non-diabetics, with an estimated 28% risk. In fact, diabetics are 2 to 3 times more likely to develop depression than non-diabetics. One in three diabetics suffers from a form of depression that is associated with dysfunction and reduced quality of life. Depression is a mood disorder characterized by symptoms of low mood, decreased energy and interest, feelings of guilt, difficulty concentrating, anorexia, thoughts of death and suicide, insomnia or hypersomnia, significant weight loss, and dysfunction. Depression in some diabetics can be a psychological response to the severe pain of neuropathy. There is also evidence that plasma glucose concentrations affect the mood of diabetic patients so that depression in diabetic patients is associated with poor glycemic control and the level of hyperglycemia is directly related to the severity of depression. Research has also shown that cerebrovascular disease and cerebral ischemia due to diabetes are often associated with depression. In mild cases of diabetes, even without obvious cerebrovascular events and recurrent attacks, the presence of CNS hypoglycemia has some degree of dysfunction. This complication initially appears as a mild cognitive

disorder and over time and increases in severity, usually in the form of depression. Visual impairment due to retinopathy, recurrent hospitalizations, and sexual dysfunction are other causes of depression in diabetic patients. Mental disorders in diabetic patients have a negative effect on blood sugar control and better results can be achieved in the treatment of blood sugar by treating depression. On the other hand, it seems that the course of depression in diabetic patients is more malignant than in other patients, and this indicates the need to pay more attention to the mood of diabetic patients and treat their depression. Nitric oxide is a reactive free radical that acts as a transmitter in several processes including neurotransmission and antimicrobial and antitumor activities. This gene encodes a nitric oxide synthase that is expressed in the liver and is induced by a combination of specific lipopolysaccharides and cytokines. The nitric oxide synthase gene with three related gene-like genes is located in the Smith-Magnesia syndrome region on chromosome 17. Nitric oxide (NO) is a messenger molecule with various functions in the body. In macrophages, nitric oxide mediates tumor and bactericidal activities. It also has nitrosylation activity and mediates cysteine-S-nitrosylation of cytoplasmic target proteins including PTGS2 / COX2. Cysteine 247 is involved in regulating the activity of the GAIT complex and possibly in multiple targets of VIM, MSN, EZR, and ANXA5. It also increases the synthesis of proinflammatory mediators such as interleukins 6 and 8 in inflammation (Jia et al., 2014). Lipopolysaccharides cause depressive symptoms by activating microglia and inducing pro-inflammatory factors such as nitric oxide, eicosanoids, reactive oxygen species, and some inflammatory cytokines such as TNF-α, interleukins, prostanoids, and leukotrienes. Large amounts of nitric oxide are produced in response to LPS by iNOS (induced nitric oxide synthase). It is a protein with 596 amino acid residues and its gene (eNOS) is located on chromosome 7 of the long arm. Nitric Oxide: NO. In 2019, Motamedi et al. Conducted a study on the effect of endurance training on angiotensin and eNOS gene expression in the heart tissue of type 2 diabetic male Wistar rats. The study population consisted of 36 male Wistar rats in Three diabetic groups with endurance training (n = 12), a diabetic control group (n = 12) and a healthy group (n = 12) were randomly placed and the expression of angiotensin and eNOS gene in these groups was evaluated using Real-Time PCR technique. Their study was a case-control study. Using statistical analysis of the data, these scientists found that the expression of angiotensin and eNOS gene in the diabetic control group compared with the healthy control group showed a significant increase. Endurance exercise reduced angiotensin gene expression. And eNOS compared with the diabetic control group. The scientists went on to argue that the expression of the angiotensin gene and the eNOS of diabetic heart tissue appear to be positively affected by endurance training (Rashid et al., 2004). In 2015, Feng et al.Investigated the protective role of sirtuin-1 against ischemic injury - myocardial reperfusion by activating eNOS in diabetic rats. They were randomly divided into control and patient groups and their study type was

case-control. Finally, the expression level of the eNOS gene was examined using the Molecular Real-STime PCR technique. They went on to argue that IRT1 protects mice against ischemia-reperfusion injury by activating eNOS in diabetic rats (Feng et al., 2015). In 2017, Biasaki et al. Conducted research on the expression of eNOS and MRP4 gene expression in high-risk type 2 NSTEMI diabetics. The study population consists of 35 sick and healthy individuals in two groups; One: NSTEMI patients with and without type 2 diabetes (n = 15) and group 2: 20 patients with type 2 diabetes without a history of ischemic heart disease and the expression of eNOS and MRP4 protein genes were examined using real-time PCR. . Using statistical analysis of the data, the researchers found that eNOS gene expression was significantly less regulated in NSTEMI patients with type 2 diabetes than in NSTEMI patients without type 2 diabetes and controls. In contrast, MRP4 gene expression is highly regulated in NSTEMI individuals without type 2 diabetes compared with controls and in NSTEMI individuals with type 2 diabetes compared with control groups. The researchers went on to argue that decreased eNOS expression and increased MRP4 expression increased cardiovascular risk in these patients (Biasaki et al., 2017). Conclusion In the present paper, it was found that eNOS gene expression increased in the case group compared to the control group, which was not statistically significant ($p>0.05$). Regarding the increase of this enzyme in the case group, it can be said that the concentration of reactive oxygen or nitrogen species such as superoxide, nitric oxide, and peroxynitrite can increase in conditions such as inflammation that inhibit the body's natural defense and antioxidant activities. In recent years, it has been shown that TB producing IL-17 plays an important role in many autoimmune diseases such as multiple sclerosis, rheumatoid arthritis, and type 1 diabetes. IL17 is a profundal cytokine whose role in diabetes is the induction of nitric oxide synthase enzyme, followed by nitric oxide release, which causes the destruction of β cells. A 2001 study by Suzuki et al. showed that serum nitric oxide levels were higher in patients with depression than those without depression. Several studies have also shown that nitric oxide synthase enzyme plays an important role in the pathogenesis of depression by producing nitric oxide. Nitric oxide is composed of L-arginine with the help of nos enzyme and in turn activates the dissolved guanylate cyclase enzyme (sGC), which is responsible for converting guanosine triphosphate (GTP) into cyclic guanosine monophosphate (cGMP). The findings suggest that excessive levels of cGMP may cause a state of depression-like and that lowering its level may cause antidepressant activities. In addition, cGMP is decomposed into guanosine monophosphate (GMP) with the help of phosphodiesterase (PDE). Therefore, in speculation, it can be said that inhibiting the phosphodiester enzyme using its inhibitors may increase cGMP levels and cause depression. Therefore, it can be concluded that increasing the expression level of this enzyme is associated with depression and is not associated with diabetes. (Suzuki et al., 2001, Lee et al., 2006) Finally, for further investigation, it is suggested that: • Use more samples to

achieve better results. • It is recommended that this test be performed on people with non-diabetic depression to clarify the ambiguities of the test.

Keywords: Gene expression, eNOS, Type 2 diabetes, Depression, Real-Time-PCR

The effect of Fenofibrate combined with α-Lipoic acid on creatinine and uric acid in rat model of non-alcoholic fatty liver disease (Research Paper)

Babak Hassankhan,[1,*] Parichehreh Yaghmaei,[2] Kazem Parivar,[3] Azadeh Ebrahim-Habibi,[4]

1. Department of Biology, Faculty of Basic Sciences, Science and Research Branch, Islamic Azad University, Tehran, Iran
2. Department of Biology, Faculty of Basic Sciences, Science and Research Branch, Islamic Azad University, Tehran, Iran.
3. Department of Biology, Faculty of Basic Sciences, Science and Research Branch, Islamic Azad University, Tehran, Iran
4. Endocrinology and Metabolism Research Center, Tehran University of Medical Sciences, Tehran, Iran.

Introduction: Background and Aim: Non-alcoholic fatty liver disease (NAFLD) connects to chronic kidney disease (CKD) and the prevalence of CKD was significantly higher in NAFLD patients. NAFLD is associated with insulin resistance and hyperlipidaemia. Insulin resistance plays an important role in metabolic syndrome and CKD. Lipoprotein abnormalities such as high triglycerides (TGs), associate with subsequent decline in kidney function. Hyperlipidemia induce oxidative stress, lipotoxicity and immune activation. Insulin resistance and hyperlipidaemia play potential pathogenic role in the development and progression of CKD. Pathogenesis of NAFLD and CKD are complicate and suggests that combination therapy may be more effective for the treatment of NAFLD and CKD. Fenofibrate is one of the most important drugs for the management of dyslipidemia and α-lipoic acid has antioxidant effect. The present study aimed to investigate the effect of fenofibrate in combination with α-Lipoic acid on kidney function and the prevention of hypertriglyceridemia and oxidative stress in rat model of non-alcoholic fatty liver disease.

Methods: Materials and Methods: Forty male Sprague-Dawley rats were divided into five groups (n=8 in each group): normal control group (NC) to receive a standard chow and four high fat diet fed groups that they received a high fat emulsion diet (HFD) alone, (HF group), and in combination with 100 mg/kg fenofibrate, (Fen group), in combination with 60 mg/kg α-Lipoic acid, (Lip group), and in combination with 50 mg/kg fenofibrate plus 30 mg/kg α-lipoic acid, (Fen+Lip group). Animal model of non-alcoholic fatty liver disease was induced by oral gavage of HFD after six weeks. Rats were simultaneously treated with fenofibrate alone and in combination with α-lipoic acid in each group. After this time, the rats were sacrificed. Blood samples were collected for measurement of biochemical parameters includ serum lipid profile, glucose, insulin, insulin resistance (HOMA-IR), liver enzymes,

creatinine, uric acid, adiponectin and tumor necrosis factor α (TNF-α). Liver tissue was homogenized for measurement of lipid profile and hepatic malondialdehyde (MDA). Liver histological tests with hematoxylin-eosin staining were performed to evaluate fat accumulation in liver tissue.

Results: Results: After six weeks, the level of lipid profile, blood glucose, insulin, insulin resistance (HOMA-IR), TNF-α, creatinine, uric acid, in serum and hepatic content of malondialdehyde (MDA), and triglyceride (TG) significantly increased (P<0/05) and serum adiponectin significantly decreased in high fat group compared to the normal control group (P<0/05). Liver sections of high fat group displayed obvious fat droplets and macrovesicular steatosis. Hepatic content of MDA was not decrease by fenofibrate (P>0.05). Fenofibrate in combination with α-lipoic acid significantly decreased the hepatic content of MDA in Fen+Lip group compared to the high fat group (P<0.05). Fenofibrate alone did not alter the serum concentrations of creatinine and uric acid in Fen group compared to the HF group (P>0/05) but fenofibrate combined with α-Lipoic acid significantly decreased the serum concentrations of creatinine and uric acid in Fen+Lip group compared to the HF group (P<0/05).

Conclusion: Conclusion: Our results indicate that fenofibrate in combination with α-lipoic acid showed higher protect effect on oxidative stress compared to the fenofibrate alone and fenofibrate with α-lipoic acid can reduc serum concentrations of creatinine and uric acid compared to the fenofibrate alone. These results suggest that combination therapy with fenofibrate and α-Lipoic might provide a beneficial method for treatment of chronic kidney disease and improvement of kidney function.

Keywords: Keywords: Non-alcoholic fatty liver disease, Chronic kidney disease, Creatinine, Uric acid, Malondia

The effect of Granulocyte Colony Stimulating Factor dose and administration interval after allogeneic hematopoietic cell transplantation on early engraftment of Neutrophil and Platelet (Research Paper)

Leila Noorazar,[1] Majid Gholizadeh ,[2] Mojtaba Shafiei,[3] Elham Roshandel ,[4,*]

1. Hematopoietic stem cell research center, shahid beheshti university of medical sciences, Tehran, Iran
2. Shahid Beheshti University of Medical Sciences, Department of Hematology and Blood Banking, School of Allied Medical Sciences Tehran, IR
3. Mashhad University of Medical Sciences Faculty of Medicine, hematology and blood banking Mashhad, Razavi Khorasan, IR
4.

Introduction: Background: Hematopoietic stem cell transplantation (HSCT) is one of the treatments for hematologic malignancies. Numerous factors affect the HSCT outcome. The purpose of this study was to investigate the effect of post-HSCT administration of granulocyte colony-stimulating factor (post-G-CSF) on early neutrophil and platelet engraftment in allogeneic HSCT (Allo-HSCT).

Methods: Material & methods: The study was performed on 76 patients diagnosed with AML and ALL. All patients underwent allo-HSCT at Taleghani stem cell transplantation center, Tehran, Iran, from February 2016 to December 2018. Chemotherapy regimens based on patients' conditions were selected between myeloablative and reduced-intensity regimens.

Results: Results: Statistical analysis revealed that the number of administered G-CSF units after HSCT was a time-dependent variable. Statistical analysis before day +11 reported that patients who received G-CSF <14 units had three times better early neutrophil engraftment than those with G-CSF ≥14 (CI 95%, AHR=3.03, p:0.002). CD3+ cells count <318.5×106/kg was associated with fast platelet engraftment (CI 95%, AHR 2.28, p:0.01).

Conclusion: Conclusion: In this study, post-G-CSF stimulation was associated with early engraftment in a time- and dose-dependent manner. Administration of G-CSF beyond 14 units resulted in adverse effects on neutrophil early engraftment. It also appeared that with a reduction in CD3+ cell counts, the likelihood of GVHD decreases, and platelet engraftment occurs earlier. Further investigations in the future are required to determine the factors affecting the process of early engraftment.

Keywords: Allo-HSCT, Post-G-CSF, Early engraftment, Neutrophil, Platelet

The effect of Injectable platelet rich fibrin (i-PRF) on inflammation in the mouse ovarian tissue after autotransplantation (Research Paper)

Sahar Hatami,[1,*] Seyed Mohammadali Shariatzadeh,[2] Malek Soleimani Mehranjani,[3]

1. Phd student, Department of Biology, Faculty of Science, Arak University
2. Department of Biology, Faculty of Science, Arak University
3. Department of Biology, Faculty of Science, Arak University

Introduction: Ovariaan tissue transplantation is only option for patiant young woman and prepubertal girls after chemotherapy and radiotherapy. Howere one of the major limitations in ovary transplantation is ischemia-reperfusion (I/R) injury that due to the production of inflammatory factors and finelly, reduction survival of transplanted tissue. Injectable platelet rich fibrin (i-PRF) is a liquid formulation of platelet rich fibrin (PRF) without the use of anti-coagulants. It contains a fibrin matrix resulted from fibrinogen molecules activation in plasma, leukocytes, circulating stem cells, platelets and growth factors. We aimed to evaluate the effect of i-PRF bioscaffold on the serum level of inflammatory factors such as interlukin 6, 10 (IL6,10) and Tumor necrosis factor-α (TNF-α) following mouse ovarian tissue transplantation.

Methods: Mice were divided into (n=6): control, autograft + saline (whole ovarian tissue transplanted in the gluteus superficialis muscle, saline directly injected into it), autograft + i-PRF (whole ovarian tissue transplanted in the gluteus superficialis muscle, i-PRF was directly injected into it). 7 days after ovary transplantation, serum concentrations of IL-6, IL-10 and TNF-α were assayed. Data were analyzed using one-way ANOVA and Tuckey's test and the means were considered significantly different at p-value < 0.05.

Results: Serum concentrations of TNF-α and IL-6 in the autograft group increased significantly compared to the control, while it showed a significant reduction in the autograft + i-PRF group compared to the autograft group. Moreover, the serum level of IL-10 was significantly lower in the autograft group when compared to the control counterpart. Whereas it showed a significant increase in the autograft + i-PRF group compared to the autograft group ($p < 0.05$).

Conclusion: Our results for the first time revealed that i-PRF bioscaffold at the graft site can decrease inflammation. therefore can prevent IR induced damages and improve the function of the grafted ovary.

Keywords: Ovarian tissue transplantation, Injectable platelet rich fibrin (i-PRF), Ischemia–reperfusion, Infla

The effect of L-carnitine on Restoration of Mice Ovarian Endocrine Function and Estrous Cycle after Autografting (Research Paper)

Khadijeh Sanamiri,[1,*] Malek Soleimani Mehranjani,[2] Maryam Shahhoseini,[3] Mohammad Ali Shariatzadeh,[4]

1. Department of Biology, Faculty of Science, Arak University, Arak, Iran
2. Department of Biology, Faculty of Science, Arak University, Arak, Iran
3. Department of Genetics, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran
4. Department of Biology, Faculty of Science, Arak University, Arak, Iran

Introduction: Despite the remarkable progress that has been achieved in the field of cancer treatment, which has increased the rate of survival in cancer patients ,but unfortunately some patients still suffer from infertility caused by chemotherapy and/or radiotherapy, affecting their life quality. Ovarian tissue transplantation is a fertility restoration technique used in these patients and one of the major obstacles of it is ischemia/reperfusion injury that leads to the depletion and apoptosis of the follicles. Therefore, reducing graft ischemia is essential for the functional support of the ovary. L-carnitine has antioxidant and anti-inflammatory properties and can therefore be used to reduce ischemic damages. The aim of this study was to investigate the effect of L-carnitine injection on the endocrine function of the transplanted mouse ovarian tissue.

Methods: The Naval Medical Research Institute (NMRI) mice at the age of 4-5 weeks, were divided randomly into groups of: control, autograft and autograft + L-carnitine (200 mg/kg daily intrapritoneal injections). 28 days after ovarian transplantation, blood samples were collected and serum levels of progesterone (P4) and estradiol (E2) were analyzed. To evaluate the restoration of the cyclic ovarian activity, daily vaginal smears were taken, beginning on day 7 post-transplantation. Data were analyzed using one-way analysis of variance (ANOVA) and Tukey test, and the means were considered significantly different at $p < 0.05$.

Results: As indicated by our results, serum concentrations of progesterone and estradiol were significantly lower in the autografted group compared to the control counterpart, whereas in the autografted + L-carnitine group, the mentioned parameters were significantly higher when compared to the autografted group. In addition, the estrous cycle recovery was more rapid in the autografted + L-carnitine group than the autografted group.

Conclusion: L-carnitine can restore endocrine function of the transplanted ovaries through reducing oxidative stress and inflammation.

Keywords: L-Carnitine, Mice, Ovarian graft.

The effect of mecamylamine on zinc oxide nanoparticles function on passive avoidance memory and locomotor activity (Research Paper)

Ahmad Sadeghi,[1,*] Niloufar Darbandi,[2]

1. Department of Biology, Faculty of Science, Arak University, Arak, Iran
2. Department of Biology, Faculty of Science, Arak University, Arak, Iran

Introduction: Zinc oxide nanoparticles due to have special properties, in many products such as cosmetics, food additives and etc, are being used. These compounds reach the brain through the blood-brain barrier or the olfactory nerve pathway and damage the brain through oxidative stress, inflammatory responses and cytotoxicity. It has been shown that zinc oxide nanoparticles can induce changes in learning ability and memory by altering synaptic plasticity. Nicotine receptors are present in various parts of the brain, including the hippocampus, and control synaptic plasticity through the release of various neurotransmitters, including acetylcholine, dopamine, and glutamate. Nicotinic receptors signaling pathways in the dorsal hippocampus may also involve in drug interactions and memory formation. In the present study, the effect of nicotinic receptors blockade in the dorsal hippocampus by mecamylamine in the effects of zinc oxide nanoparticles on passive avoidance memory and locomotor activity was investigated.

Methods: In this experimental study, adult male Wistar rats weighing 220-250 g were divided into control groups (saline 1 ml/kg), zinc oxide nanoparticles (0/5 mg/kg), mecamilamine (0/5 and 1 µg/rat) and mecamilamine (0/5 and 1 µg/rat) along with zinc oxide nanoparticles (0/5 mg/kg). In all groups, bilaterary cannulated was performed in CA1 region. Intracerebral injection of saline or mecamilamine immediately after training and intraperitoneal injection of saline or zinc oxide nanoparticles with 5 minutes interval was performed. Passive avoidance test was used to assess memory 24 and 72 hours after training. Motor activity was assessed at each stage after the behavioral test.

Results: post-training injection of zinc oxide nanoparticles (0/5 mg/kg) had no significant effect on passive avoidance memory compared with control group ($p>0/05$). Intrahippocampal injection of mecamylamine combined with ineffective dose of zinc oxide nanoparticles (0/5 mg / kg) dose-dependently decreased memory retrieval compared with the control group ($p<0.001$). Compared with control group, injection of mecamylamine alone had no effect on long-term memory ($p>0/05$). Measurement of locomotor activity in experimental groups did not show a significant difference with control group ($p<0/05$).

Conclusion: According to the results, it seems that zinc oxide nanoparticles reduce memory function by reducing the activity of the nicotinic cholinergic system in the CA1 region of the dorsal hippocampus. This effect may be directly or indirectly mediated by other neurotransmitters.

Keywords: Dorsal hippocampus, Locomotor activity, Mecamylamine, Memory, Zinc oxide nanoparticles

The effect of nonsteroidal anti-inflammatory drug (NSAID) celecoxib on the structure of human hemoglobin (Research Paper)

Katayoun Kebriti,[1] Mina Sadat Naderi,[2] Seyed Mehdi Tabaie,[3,*]

1. Department of Medical Laser, Medical Laser Research Center, Yara Institute, ACECR, Tehran, IRAN
2. Assistance Professor, PhD of Biophysics, Department of Biophysics, Faculty of Biological Sciences, Islamic Azad University, Tehran North Branch, Tehran, IRAN
3. Associate Professor, MD of Dermatology, Department of Medical Laser, Medical Laser Research Center, Yara Institute, ACECR, Tehran, IRAN

Introduction: Human hemoglobin, probably more than any other molecule, has allowed the birth and maturation of molecular medicine. Hemoglobin (Hb) is a globular tetrameric protein found in red blood cells. Hemoglobin is a two-way respiratory carrier. Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most common pain relief, anti-inflammatory and analgesics medicines approved by FDA. There are currently more than 50 different types of NSAIDs on the world market. NSAIDs are divided into two groups of selective and non-selective. Due to the common use of these drugs and the abundant protein importance of hemoglobin, the possibility of structural changes by celecoxib on hemoglobin was investigated.

Methods: The study in-vitro. The structural changes of hemoglobin with different concentrations of celecoxib treatments (10-1000 µM) were studied. The changes were detected by UV-visible spectrophotometry

Results: The results showed celecoxib can cause structural changes in hemoglobin. With increasing in celecoxib concentration, the hemoglobin becomes unfolded. Also, concentrations of 50, 100 and 200 µM are optimal concentrations for celecoxib, which cause fewer changes than higher concentrations of this drug.

Conclusion: Due to the widespread diseases of hemoglobin and the importance of its stability and extensive worldwide use of NSAIDs such as celecoxib, the effects of these drugs on the structure of hemoglobin could lead to a new approach of treatment.

Keywords: Hemoglobin, nonsteroidal anti-inflammatory drugs (NSAIDs), Structure

The effect of overweight and obesity on female infertility (Review)

Sedigheh solgi,[1,*] zeinab sadat moosavifard,[2]

1. BSc in Nursing, Department of Nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.
2. Department of Nursing, faculty of nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.

Introduction: Infertility means the inability to conceive or the inability to maintain a pregnancy after 6 months to a year of trying to conceive, and various factors play a role in causing infertility, one of which is obesity and overweight. Obesity is a major health problem. In many developed countries, 14 to 20 percent of women of childbearing age are obese BMI ›30, while in other countries the prevalence is reported to be 60 percent. Obesity has a negative effect on women's reproductive health because it is associated with an increased risk of menstrual disorders, anovulation and infertility.

Methods: In this study, a search was performed using search engines inical key, scopus, pubmed and articles from 2014 to 2019 were reviewed.

Results: Based on the findings, we found that weight gain in women increased the prevalence of polycystic ovaries, irregular menstrual cycles, infertility, miscarriage and failure in infertility treatments, and even pregnancy problems such as gestational diabetes, preeclampsia, such macrosomia, and cesarean delivery. Is in touch. Obesity with hormonal imbalance interferes with normal ovulation and can cause infertility in women. Studies have shown that weight loss improves ovulation. Obesity, which is associated with the prevention of ovulation and infertility in women. In case of pregnancy, it has a detrimental effect on the health of the fetus and mother, such as hyperlipidemia, metabolic syndrome and gestational diabetes, and all of these cases place a great economic burden on the mother, family and community. Fetal and neonatal complications caused by maternal diseases and diabetes due to obesity are very widespread and costly. As the body mass index increases, the response to infertility treatments decreases. And the costs of treating infertility in obese women are very high.

Conclusion: Because studies have shown that weight loss and lifestyle management can improve the fertility of women with obesity, obesity management by lifestyle modification is recommended for these people before infertility treatments.

Keywords: Pregnancy, obesity, infertility

The effect of parental rejection on the incidence of social anxiety disorder in children (Research Paper)

Iman Mosalanezhad,[1,*] Saeid Askari,[2] Raha Sadeghi,[3] Roza Sadeghi,[4] Zeinab Sadat Moosavi Fard,[5]

1. Master of Educational Sciences in Primary Education
2. Master student of clinical psychology, Shiraz Azad University
3. Master of Persian Literature
4. Master of Sociology
5. Department of Nursing, Faculty of nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.

Introduction: The characteristics of family members, especially parents, can affect a child's behavior. This study aims to investigate the effect of parental rejection on the development of social anxiety disorder in children. The present study evaluates its importance and fundamental role.

Methods: In this descriptive-analytical study, 300 patients aged 5 to 11 years in outpatient medical centers in Shiraz in 2009-2010 were easily selected and their behavioral disorders were diagnosed by a psychiatrist. The long type of NEO personality questionnaire was completed for their parents and then the data were analyzed by independent t-test, analysis of variance and analysis of covariance.

Results: Anxiety disorders in children with aggression, flexibility, striving for success, self-control, caution in decision making and total test score of parents and child mood disorders with altruistic traits, order, striving for success and caution in decision making and agitated behavior disorders with positive emotions Imagination, emotions, striving for success and the total score of the parents' test and the child's defecation were significantly associated with parental self-control ($P < 0.05$). Most people want to socialize and many people want to be accepted by society. Rejection can provoke negative feelings and emotions in a person. For the child, the parents are considered as a shield against the calamities of the times, the parents are the source of safety and physical and mental satisfaction of the child, so the love of the parents can help the child's development in the same way. The problem of social anxiety disorder is one of these research findings that plays a major role in the large-scale impact of parental rejection and their acceptance on the formation of children's personality.

Conclusion: Childhood behavioral disorders such as anxiety are associated with the type of personality traits of parents.

Keywords: parental , rejection, social anxiety , disorder, children

The effect of resveratrol in comparison with cisplatin on cytotoxicity and production of reactive oxygen species in a prostate cancer cell line (LNCap) (Research Paper)

Nasim kojoeiyan Jafari ,[1,*] Mohammad Taghi Goodarzi,[2]

1. Department of Biochemistry, Islamic Azad University, Shahrood Branch, Shahrood, Iran
2. Department of Biochemistry, Islamic Azad University, Shahrood Branch, Shahrood, Iran

Introduction: Objective Prostate cancer is one of the most common diseases worldwide, and many efforts are made to treat that. However, no absolute treatment is recognized for the disease. Accordingly, this study tends to investigate the effects of resveratrol in comparison with cisplatin on the cytotoxicity and production of reactive oxygen species (ROS) in a prostate cancer cell line (LNCap).

Methods: Methods After treatment of LNCap cells with concentrations of 1, 10, 100, and 1000µg/ml of resveratrol, and 1, 5, 10, and 50µg/ml of cisplatin, the viability percentage of cells was analyzed using MTT and spectrophotometry methods. Also, the reactive oxygen species (ROS) production in this cell line with a concentration of IC50 cisplatin and resveratrol was analyzed using the flow cytometry (FC) method.

Results: Results The results of MTT test showed that cisplatin and resveratrol can both reduce the cell viability in high concentrations because of increased cytotoxicity. Measurement of ROS production level showed that cisplatin and resveratrol increased ROS levels compared to control cells.

Conclusion: Conclusion The results obtained from this study showed that resveratrol as a plant derivative has anticancer and antioxidant properties. According to the side effects of cisplatin, it can be replaced by resveratrol as a good candidate to be used in chemotherapy.

Keywords: Keywords: prostate cancer, resveratrol, cisplatin, reactive oxygen species (ROS)

The effect of SARS-CoV-2 variants on the efficacy of COVID-19 vaccines (Review)

Mohammad Shayestehpour,[1,*] Mehrdad Mohammadi,[2]

1. Department of Microbiology and Immunology, Faculty of Medicine, Kashan University of Medical Sciences, Kashan, I.R. Iran
2. Department of Microbiology and Immunology, Faculty of Medicine, Kashan University of Medical Sciences, Kashan, I.R. Iran

Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel viral agent that can cause a life-threatening respiratory disorder named coronavirus disease 2019 (COVID-19). Several protein subunit COVID-19 vaccines have been proposed for use in humans. The major concern is the efficacy of subunit vaccines and elicited antibodies to neutralize the different SARS-CoV-2 variants. This review is focused on the impact of spike mutated variants of SARS-CoV-2 (B.1.1.7 (Alpha), B.1.351 (Beta), P1 (Gamma), B.1.617 (Delta) and C.37 (Lambda) on the efficacy of subunit recombinant vaccines.

Methods: Independent searches in PubMed, Web of Science, Scopus, and Global Index Medicus were conducted by two researchers. The search strategy consisted of a word combination covering the following areas (COVID-19 OR SARS-CoV-2) AND Vaccine AND B.1.1.7 Variant OR B.1.351 variant OR B.1.1.28.1 Variant OR B.1.617.2 OR C.37 variant. The search had no geographic or language restrictions and included all studies reporting on efficacy of SARS-CoV-2 vaccines against variants Alpha, Beta, Gamma, Delta, and Lambda.

Results: Xiu et al. revealed that UK and Brazil variants have no significantly decreased effect on vaccine impact and neutralization by sera from vaccinated individuals after two doses of BNT162b2 (Pfizer). SARS-CoV-2 vaccine NVX-CoV2373, produced by Novavax is based on S protein derived from the SARS-CoV-2 Wuhan reference strain, has shown 85.6% efficacy against the B.1.1.7 variant (95.6% against the original strain). However, in a study in South Africa Callaway et al. reported a 49.4% efficacy against B.1.351 variant in the overall population. These interim data evidence a significant decrease in vaccine efficacy influenced by variants such as B.1.351. In a study, B.1.1.7 remained sensitive to neutralization, albeit at moderately reduced levels, by serum samples from convalescent individuals and recipients of an mRNA vaccine (Moderna) and a protein nanoparticle vaccine (NVXCoV2373, Novavax). Wu et al. found no considerable impact in the neutralizing potency of sera from people who received the Moderna vaccine against the B.1.1.7 variant. Nevertheless, Wang et al. reported that B.1.351 variant was particularly more resistant to neutralization in people

immunized with Pfizer or Moderna vaccines. Wilfredo et al. analyzed neutralization potency in individuals who received one or two doses of either BNT162b2 or mRNA-1273 vaccines, suggesting that a relatively small number of mutations, like B.1.351 can mediate potent escape from vaccine responses. Shinde et al. reported on a comprehensive analysis of the NVX-CoV2373 vaccine in 4387 participants. They revealed that efficacy against B.1.351 was 51.0%. Mlcochova et al. showed evasion of the Delta variant from neutralizing antibodies present in convalescent patients, as well as in vaccinated individuals with two different vaccines in the UK (adenovirus vector (ChAdOx-1), and the other mRNA 19 (BNT162b2)). They demonstrated a reduced susceptibility of Delta to vaccine-elicited neutralization. In their data, the variant showed approximately 8 to 20-fold reduced sensitivity to vaccine-elicited antibodies. In another report by Davis et al., reductions in the neutralization of B.1.617.1 and B.1.617.2 were 4.31- and 5.11-fold, respectively. In another report, Lustig and et al. demonstrated significant fold change reduction in neutralizing titers: Gamma (P.1) 2.3, Beta (B.1.351) 10.4, Delta 2.1, and Lambda 2.6. The fold reduction of the Alpha (B.1.1.7) variant was not significant. Acevedo et al. observed greater infectivity mediated by the Lambda spike protein compared to D614G (lineage B) or Alpha and Gamma variants. In addition, neutralization was reduced by 3.05-fold for the Lambda variant, 2.33-fold for the Gamma variant and 2.03-fold for the Alpha variant. Tada et al. showed an average 2.3-3.3-fold reduction of antibody titers against Lambda variant.

Conclusion: Subunit vaccines with strong immunogenic capacity can efficiently elicit host immune response. However, the major healthcare concern is a reduction of subunit vaccines efficacy in translated by lower antibody neutralization potency against SARS-CoV-2 Alpha, Beta, Gamma, Delta, and Lambda variants. To date, low or no significant impact on vaccine efficacy against Alpha variants has been reported. Concern about and Delta, Beta, Gamma, and Lambda mutations on vaccine efficacy and treatments is greater than for the Alpha variant.

Keywords: COVID-19, SARS-CoV-2, Variant, Mutation, Vaccine

The effect of stress and anxiety during pregnancy on maternal and infant health: A review study (Review)

Sedigheh solgi,[1,*] zeinab sadat moosavifard,[2]

1. BSc in Nursing, Department of Nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.
2. Department of Nursing, faculty of nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.

Introduction: The most common mental disorders during pregnancy are anxiety and depression that cause negative consequences of pregnancy on mother and baby. The aim of this study was to identify the effect of stress and anxiety during pregnancy on maternal and infant health with the aim of giving birth to a healthy baby from a healthy mother.

Methods: To collect studies, without time limit, electronic search of internal databases, including Jihad University SID, Magiran National Database, Normagas and Elmnet, with keywords of anxiety, pregnancy depression, mental health, infant and external databases including ISI. , PubMed Google scholar and Scopus with keywords, depression, pregnancy, mental health, infant, baby, neonatal, anxiety.

Results: In the reviews, 97 articles were found, 26 of which were in line with the purpose of the research, and a review was selected to write this review study. The results showed that the effect of maternal stress and anxiety caused complications such as increased risk of allergic diseases, asthma, eczema, delayed motor and mental development, decreased growth index, nervous system development, low Apgar score, premature birth, anemia, birth of a baby Weight loss, decreased mental health, restlessness, malnutrition, insomnia in infants. Also reduced natural childbirth, premature delivery, spontaneous abortion, difficult and long labor, increased labor pain, chronic hypertension, apnea site infections, decreased milk production and secretion, decreased self-esteem, depression, mood disorders from These include the effects of pregnancy anxiety and stress on the mother.

Conclusion: Anxiety and depression during pregnancy, especially during pregnancy, can have long-term effects on the physical health and behavioral and psychological issues of mother and baby.

Keywords: Anxiety, depression, pregnancy, outcome

The effect of tomato stem extract on HPV virus (Review)

Paniz Sanjari,[1,*]

1. farzanegan 5 highschool

Introduction: Papilloma virus is the causative agent of warts in humans. Papillomavirus is from the Papovaviridae family. Wart treatment is often difficult and long-term. Tomato is a plant with high antioxidant properties that is used in the treatment of many diseases. Tomato stems are used in the treatment of warts in northwest of Iran. In this study the therapeutic effect of tomato stalk (Solanum lycopersicum) on warts was investigated.

Methods: The study was performed by culture of HPV virus and the use of human samples. A total of 15 human samples were randomly divided into three groups. 5 patients were tested by tomato stalk and 5 by tomato stalk extract. Five control samples were considered. Patients were evaluated for side effects after completing the course for two years. On the other hand, in the cell culture assay, breast cancer cells were cultured as basal medium. The effect of tomato stem extract on HPV virus and cancer cells was investigated.

Results: At the end of the course, three people in the first group were completely cured within a week and two people in the first group were cured within ten days. Also, two people in the second group were completely cured within a week, one was cured within eleven days. Two recovered completely in fourteen days. One in the third group recovered within two months. Since the third group did not use any therapies, the person's recovery could be related to the person's immune system. Also in laboratory samples, about 72% of the viruses cultured in the vicinity of tomato stem extract were killed. Nearly 69% of cancer cells are prevented from growing. No improvement was seen in the control group during the experiment.

Conclusion: Research has shown that tomato stems have an effective and rapid role in removing warts. Also, tomato stems have been effective in preventing the growth of HPV. Due to the antioxidant and antitumor properties of tomatoes, it appears that these properties in tomato also play an important role in wart destruction and HPV growth.

Keywords: Medicinal Plants, Solanum lycopersicum, HPV, Warts

The effects of hydro-alcoholic extract of Echinophora platyloba on the expression of morphine conditioned place preference in mice (Research Paper)

Parisa Valatabar,[1,*] Shiva Khezri,[2] Amir Abbas Barzegari,[3]

1. Department of Biology, Faculty of science, Urmia University, Urmia, Iran
2. Department of Biology, Faculty of science, Urmia University, Urmia, Iran
3. Department of Biology, Faculty of Basic Science, University of Maragheh, Maragheh, East Azerbaijan province, Iran

Introduction: Morphine addiction is a critical health problem. One of the main reasons for morphine abuse and addiction is the rewarding effects of this drug. Echinophora platyloba is an indigenous Iranian plant. This plant has shown analgesic effects that are possibly mediated through opioid receptors. Therefore, the purpose of the present research was to evaluate the possible interference of the hydro-ethanolic extract of this plant on morphine's rewarding effects.

Methods: Sixteen groups of mice (n=8) were used in the experiments. Conditioned place preference (CPP) method was used for the evaluation of rewarding effects of morphine (0, 1, 2.5, 5, 10, 15, and 20 mg/kg, s.c.) or the plant extract (0, 12.5, 25, 50, and 100 mg/kg, i.p.) in the mice. Additionally, in the expression experiment, five groups of mice were conditioned with the effective dose of morphine (15 mg/kg). Then, on the test day of the CPP procedure, the plant extract (0, 12.5, 25, 50, and 100 mg/kg, i.p.) was administered one hour before the test.

Results: Both morphine and the plant extract could induce a significant conditioned place preference. Moreover, administration of the plant hydroalcoholic extract on the test day could reduce CPP with an effective dose of morphine.

Conclusion: Hydroalcoholic extract of Echinophora platyloba may interfere with the rewarding effects of morphine. Therefore, this plant may have therapeutic applications in the treatment or prevention of morphine addiction.

Keywords: Morphin , Echinophora platyloba, Conditioned place preference, Mice

The effects of Mesenchymal stem cells (MSCs) on improving the respiratory status of patients with COVID-19 (Review)

Seyed Mohammadmahan Mirnasiri,[1,*]

1.

Introduction: As we already know coronavirus has spread in the world for over 2 years and unfortunately according to the statistical reports, approximately 5 million lives have been lost due to this contagious viral infection. The control and eradication of this epidemic have been taken into account as one of the most important priorities in human communities. Considering the high incidence of this disease, the need for finding an efficient treatment or medication seems necessary.

Methods: None of the suggested treatments has still been approved and finalized and all are being surveyed in clinical trials. However, the obtained results are perceived to be promising. One of these suggested treatments is based upon using umbilical cord mesenchymal stem cells to improve respiratory distress. By intravenous or intratracheal injection.

Results: Li Xu (Nanjing University School of Medicine, Nanjing, China, 2020) in a study revealed that in a group of patients being treated with mesenchymal stem cells, the rate of improving the sign and symptoms has been enhanced. In this group, clinical symptoms including fatigue and shortness of breath have been alleviated from day 3 of mesenchymal stem cells injection. On day 7, the general condition of these patients was significantly different from the control group. Giacomo Lanzoni et. al (May 2021) accomplished a clinical trial at the Division of Cellular Transplantation at the University of Miami Miller School of Medicine in the United States. They declared that Intravenous injection of MSCs dramatically alleviated the adverse effects of the disease within 6 days. This treatment was associated with increased survival of inflammatory cytokines in treated patients. The results of the second phase of the trial carried out in the Division of Infectious Diseases of National Clinical Research Center for infectious diseases, Beijing, China demonstrated a numerical improvement in the total volume of the lung lesion for 28 days, compared with placebo. A randomized controlled trial conducted in the Stem Cell Medical Technology Integrated Service Unit, Jakarta, Indonesia (Sep 2021) indicated that intravenous injection of stromal mesenchymal cells as an adjuvant in critically ill patients resulted in the control of cytokine storm. Cytokine release which is observed in patients with COVID-19 as a systemic inflammatory response syndrome is highly likely to decrease by using mesenchymal stem cells. Having said that, according to a systematic review performed by the researchers working in the pain medicine team at Mayo Clinic, USA), the intravenous or intratracheal injection presumably alleviates

minor symptoms of coronavirus infection. However, researchers also emphasize that the type of treatment modulates the inflammatory process as well as regenerates the alveolar-capillary barriers. In an exploratory clinical trial conducted at the Infectious Diseases Clinical Research center, Zhejiang University School of Medicine (ZUSM), Hangzhou (China, 2021 Feb), the efficiency of employing mesenchymal stromal cells derived from human menstrual blood has been appraised in critically ill patients with covid-19 and acute respiratory distress syndrome. 26 patients included in the experimental group received three 9 × 10 injections. This clinical trial indicates that the death toll has reduced nearly 69% in the treated group and chest imaging results in the experimental group have been improved within the first month after the injection. Some surveys have been performed in Iran as well. Iranian Registry of Clinical Trials(IRCT) has declared that an MSC-based clinical trial is ongoing in Shariati Hospital, Tehran, under the supervision and cooperation of Tehran University of Medical Sciences. However, no report from the obtained results has been published yet.

Conclusion: Since the study on the therapeutic approaches for COVID-19 treatment is ongoing, the hypothesis of the efficiency of using mesenchymal cells in patients with COVID-19 is not still clear. There are some disagreements. Nevertheless, MSC-based treatments seem to be taken into account as a promising approach to treat critically ill patients with COVID-19. Since the study on the therapeutic approaches for COVID-19 treatment is ongoing, the hypothesis of the efficiency of using mesenchymal cells in patients with COVID-19 is not still clear. There are some disagreements. Nevertheless, MSC-based treatments seem to be taken into account as a promising approach to treat critically ill patients with COVID-19. Since the study on the therapeutic approaches for COVID-19 treatment is ongoing, the hypothesis of the efficiency of using mesenchymal cells in patients with COVID-19 is not still clear. There are some disagreements. Nevertheless, MSC-based treatments seem to be taken into account as a promising approach to treat critically ill patients with COVID-19.

Keywords: Mesenchymal stem COVID-19 Respiratory status

The effects of prebiotics on the proliferation and survival of probiotic bacteria and its effect on strengthening the immune system to fight the corona virus disease. (Review)

Afagh shams,[1] Shakila shams,[2,*]

1. Eighth grade student, hazrat Zeinab talents high school.
2. Seventh grade student, hazrat Zeinab talents high school.

Introduction: Since the outbreak of Covid 19 disease, humans have been looking for ways to prevent it. Strengthening the immune system is one of the main ways to prevent pandemic diseases such as Covid 19. Recently, the use of probiotics to improve digestion and immunity has been considered in the dairy industry. The aim of this study was to investigate the effects of prebiotic fructooligosaccharide prebiotic on the growth and persistency of the probiotic bacterium "Bifidobacterium" and to investigate the different properties of the resulted synbiotic yogurt.

Methods: This study was conducted in the year 1399. In evaluating the effects of prebiotics, dilution of probiotics and prebiotic bacteria containing yogurts was performed with using Ringer's solution. To cultivate, birch agar medium containing mupirocin was used. Growth curve and retention curve as well as sense evaluating were recorded in the presence of different concentrations of prebiotics.

Results: The results showed that the growth of probiotic bacteria in the presence of prebiotics increased 10 times. At the standard level of probiotic bacteria in yogurt (1,000,000 colonies /ml), probiotics yogurt had a shelf life of 10 days,but Sinbiotic yogurt retains its beneficial effects for 15 days.

Conclusion: According to the findings of this study, the prebiotic "fructooligosaccharide" has some direct effects on increasing the growth and persistence of the probiotic bacterium "Bifidobacterium" in yogurt. As the results, it has significant effects on strengthening the immune system, in order to fight against Covid 19 disease. Synbiotic yogurt is recommended for daily consumption.

Keywords: Probiotics yogurt, Peribiotics, Synbiotics yogurt,Bifidobacterium bacteria, Fructooligosaccharide.

The Effects of Sleep Deprivation on Brain Function (Review)

Amin Vafaei poursorkhabi,[1,*]

1. Azadegan High School

Introduction: An adult needs 8 hours of sleep in a day. Numerous events such as, among other things, the secretion of different hormones, a significant increase in the performance of the immune system, the regulation of neurotransmitters, and a decrease in blood pressure occur during those 8 hours. If humans do not sleep enough, their bodies cannot function well, and this can bring about many diseases such as the weakening of the immune system, high blood pressure, neurological disorders, etc. Moreover, sleep deprivation has direct effects on the brain. Numerous events such as the control of the vital bodily functions, the secretion of different hormones, the reduction of the performance of neurons, etc. occur while a person is sleeping, and sleep deprivation can have major debilitative impacts on the brain. The current study aimed to deal with the effects of sleep deprivation on brain function.

Methods: Several activities are performed while a person is sleeping. Regulating the neurotransmitters is ones of such activities. Hormones including noradrenaline (norepinephrine), serotonin, and dopamine are the neurotransmitters of the human body that are regulated during sleep. Thus, sleep deprivation can disturb the regulation of neurotransmitters and bring about symptoms such as aggression, depression, and hallucination. Furthermore, blood pressure and heartrate decrease during sleep. Sleep deprivation can disturb this cycle and bring about tachycardia and high blood pressure. Recent studies have proven that sleep deprivation can increase the risk of cancer. In addition, it can lead to slackness and the pain and weakness of muscles. Sleep deprivation has a direct effect on the immune system. While a person is asleep, the immune system significantly increases its activity and fights infections. This process is disturbed by sleep deprivation, and the immune system gets weakened against environmental factors. In addition, sleep deprivation has a direct impact on the nervous system, particularly on brain. It can result in aggression, reduced understanding, neurological disorders, diplopia, etc. by reducing the function of neurons in the long run. It can also reduce the efficiency of the cerebellum, which can result in vertigo, the lack of balance, etc.

Results: Sleep deprivation has many indirect effects on the brain in addition to its direct effects. For instance, neurological messages are not delivered appropriately when the regulatory cycle of neurotransmitters is disturbed. This can bring about aggression, neurological disorders, and an increase in the possibility of depression. Furthermore, a sudden increase in blood pressure

and heartrate can lead to a stroke. Sleep deprivation can disturb the secretion of growth stimulators such as somatotropin, thyrotropin, corticotrophin, lactogen, and gonadotropin. Sleep deprivation can reduce the performance of the cerebellum, and it has frequently been observed that a sleep-deprived person shows symptoms such as vertigo, the lack of balance, limp, and sometimes inability to walk. Sleep deprivation can bring bout mental and psychological disorders such as depression, hallucination, aggression, and temporarily disturb senses such as weakened smelling, diplopia, hearing terrible noises, the feeling of being called by others, feeling extreme heat, becoming intolerable to heat, and being unable to recognize tastes by reducing the function of brain neurons. In addition, sleep deprivation can reduce brain function and weaken understanding and IQ. While body and brain can adapt to a few days of sleep deprivation, long-term sleep-deprivation will bring about irremediable effects and consequences.

Conclusion: Since sleep deprivation has a direct and negative effect on the brain, it can reduce the level of understanding and IQ. Sleep deprivation can also lead to the emergence of mental and psychological disorders such as hallucinations. It can also disturb the senses. Moreover, it can disturb the function of the cerebellum, which will bring about consequences such as inability to maintain one's balance.

Keywords: Sleep Deprivation, Brain, Neurotransmitters, Cerebellum, Neuron.

The evaluation of the effects of Wharton gel mesenchymal stem cells with traditional medicine in the treatment of skin lesions caused by burns (Review)

hediyeh mohamedi,[1,*] Hamideh Abnoos,[2]

1. , Mashhad, Khorasan Razavi, Om al banin state model high school
2. Mashhad Khorasan Razavi biology teacher

Introduction: Burns are one of the most devastating injuries and major concerns of the World Health Organization (1, 2). It is the fourth most common injury after car accidents, falls and interpersonal violence. More than 300,000 people die from burns each year. Millions of people suffer from disabilities and social, psychological and economic disabilities caused by burns (4). Burns are injuries to the flesh or skin caused by heat, electricity, chemicals, friction, or radiation and can be associated with emotional and psychological disorders. In full-thickness burns or third-degree burns, all layers of the skin are damaged and the treatments required depend on the severity of the burn (5). It is also known as one of the main causes of skin tissue damage, which in addition to increasing vulnerability to the entry of foreign factors, causes dehydration and natural shape of the skin (7). In general, the burn repair process includes a set of cellular, molecular and tissue processes (8). In fact, wound healing is a four-step overlapping process involving the stages of coagulation, inflammation, fibroplasia, and tissue change. In the coagulation phase, diapause begins as a result of vasoconstriction and the release of catecholamines. In the inflammatory phase, the wound is occupied by phagocytic cells. In the fibroplasia phase, fibroblasts that have migrated to the wound synthesize and secrete different types of collagen, resulting in increased wound strength, and angiogenesis occurs at this stage. In the stage of changing the tissue arrangement, the tissue returns to its natural state (3). According to these studies, it seems that the use of new methods such as cell therapy as a non-invasive approach can be a good alternative to old methods of treatment. Cell therapy is an interesting and effective strategy in the treatment of diseases and includes the replacement of stem cells or tissue made from stem cells for various diseases and injuries. So far, various stem cells have been used in the treatment of diseases through various researches. Gone (6). Vinegar is an aqueous solution of acetic acid and other chemicals that may contain flavorings. Acetic acid is usually 5 to 20% of the volume of vinegar. Acetic acid is usually produced by the fermentation of ethanol or sugar by acetic acid bacteria. Natural vinegar has less tartaric acid and lemon essence. Ordinary vinegar, in addition to removing natural antibiotics, contains biological amino acids after fermentation, while synthetic vinegar does not contain this important substance. Natural vinegar regulates the body's metabolism because it secretes saliva secretion. Increases saliva secretion. According to

biochemistry, it has a large amount of protein (albumin) that better digest and digest food. Mixing vinegar with saliva also protects teeth from decay. Vinegar is a body stimulant and is considered an antipyretic for some medications, such as atropine. Vinegar has long been considered a carcinogen, but is now considered to be partly a carcinogen. In a salt diet (salt loss and not eating it), it is good to eat vinegar because vinegar removes the salt in fruits. It stimulates and increases and excretes the body through sweating. The same goes for the meat diet, and it is not only suitable for people with liver disease. Vinegar is very useful for preventing obesity and weight loss as well as in anti-diabetic diet (33). It should be noted that white vinegar contains acetic acid (a component of aspirin), which can help relieve pain, itching and inflammation caused by burns, and as a disinfectant closes open pores of the skin. Prevents infection and inflammation at the site of the defect. (30). A stem cell is a cell with a high ability to divide that has not yet divided. Cells from mitotic division make more stem cells and can differentiate into other types of cells, and some, such as nerve cells, may lose the ability to divide during the process of differentiation. In mammals, there are two broad types of stem cells: embryonic stem cells and adult stem cells. In adult organisms, stem cells act as a repair system for the body and regenerate adult tissues. Today, the use of these cells to repair damaged tissues is expanding. Stem cells are divided into all (full), multipotent, multipotent and monopotent (26) based on their ability to make different tissues (26). The rate of angiogenesis and the development of blood vessels is actually one of the most effective factors in wound healing. It also prevents the burn wound from deepening. If an agent such as a drug can accelerate the formation of blood vessels through biochemical and pharmacological mechanisms and be able to alter tissue circulation in the burn area, it will repair (9). The use of stem cells in tissue regeneration programs due to The ease of replication and isolation in vitro and their potential ability to advance and accelerate the healing process of tissue damage through the production of multiple growth factors have received much attention (12). Today, umbilical cord Wharton jelly stem cells have been considered as a suitable cellular source. The reason for using these cells is easy access, low cost, lack of invasive methods in separating tissue from the donor, the ability to differentiate into different cells and abundant sources of these cells (10). The umbilical cord consists of two arteries and a umbilical vein, both of which are located in a special mucosal connective tissue called the Wharton jelly, which is covered by the amniotic epithelium. The umbilical cord of hospital waste is considered and access to these cells is a non-invasive method. In addition, access to umbilical cord mesenchymal stem cells is not cumbersome and has no moral problem. Umbilical cord mesenchymal stem cells have a separate capacity for self-renewal. , While retaining their plurality and high differentiation ability, although some of these differentiation abilities are known in part (11, 13). Umbilical cord mesenchymal stem cells have received a great deal of attention due to their immunomodulatory properties. Today, mesenchymal

stem cells have been proposed as a suitable source for medical resuscitation and immunotherapy (14). In 2019, Nazempour et al. Used human umbilical cord Wharton jelly stem cells to treat a burn pattern in rats. (16). The amniotic membrane is the innermost layer adjacent to the fetal amniotic fluid, which today is mainly excreted in the country as a biological waste. It has established itself in restorative medicine with numerous companies around the world processing and mass-supplying this biomaterial. (28) Combining traditional Iranian medicine with modern therapies can be a very effective idea for treating various diseases. It should be noted that reports from the World Health Organization confirm that more than 80% of the world's population still uses traditional medicine and herbs to treat a variety of diseases. Today, in some parts of Iran, a combination of animal oil and coriander gum is used to treat burns. Pistoia Atlantic is one of the wild pistachio species in Iran that is grown by car in many parts of the country, especially in the Zagros region (15). In traditional Iranian medicine, this plant and its gum are used in many cases, including in the treatment of stomach problems, infections, eczema, asthma, and as an anti-inflammatory, anti-viral and anti-bacterial. Coriander gum contains compounds such as fatty acid compounds, transbernol and pinene, which have been studied in relation to their biological activities, especially antimicrobial (18, 17). Sheep animal oil is also rich in unsaturated fatty acids, which are traditionally used in some parts of Iran to repair burns (19). Researchers at Iran University of Medical Sciences studied the effect of animal oil on the healing of second-degree burn wounds in rats (37). It should be noted that potatoes are the first treatment in the list of traditional and home remedies for burns. Raw has soothing properties and prevents skin irritation. In this way, it can prevent the formation of unpleasant blisters. And mixed water, which is marketed as vanilla extract, which generally contains 35% alcohol. Vanilla extract may also contain sugar, corn syrup or propylene glycol. The most famous use of this plant in Iran is in confectionery and ice cream. The Tutankhamun Indians were the early makers of vanilla. Vanilla beans contain 1-2% vanillin (4-hydroxy-3-methoxybenzaldehyde). Most of the vanilla flavor is due to the presence of vanillin in it. Vanillic acid, p-hydroxybenzoic aldehyde, tannins, polyphenols, free amino acids and resin are other components of this plant (34, 35) Vanilla is the most expensive spice after saffron. Of course, vanilla extract or essential oil can be used for minor burns (30)

Methods: In one study, acrylic acid at different concentrations was bonded to the silicone film at different concentrations after activating the surface of the silicon film by two-step plasma method. Chitosan and gelatin were then fixed in different percentages on the samples. Surface properties were evaluated by Fourier transform infrared spectroscopy and contact angle measurement. Finally, adhesion, dispersion and number of L929 cells on the samples were studied (9). But also a study to prove the effect of animal oil on burns: This study is an experimental type and was conducted in 2013 in the animal

laboratory of Hazrat Fatemeh Hospital in Tehran. Thirty-six adult male Sprague-Dawley rats weighing approximately 250-300 g were selected and kept in accordance with the animal rights standard and the agenda of the Medical Ethics Committee on the use and care of laboratory animals at Iran University of Medical Sciences. Thus, they were kept in standard separate cages with a light cycle of 12 hours of darkness and 12 hours of light and a temperature of 22-24 ° C. During this time, the animals had sufficient access to water and food. 60 mg / kg), the hairs on the back of the rats were shaved with an electric shaver. Then, to create a deep second degree burn on the back of the rats, 2 cm 2 cm metal stamps placed in boiling water at 90 ° C for three minutes were placed in contact with the skin on the back of the animal for eight seconds. Rats were randomly divided into three groups. In the first group with a thick layer of ointment with a diameter of 2-3 mm, the second group with a layer of animal oil and the third group with Vaseline were treated daily. Every five days, the burn site was photographed near the ruler using a Nikon D300digital camera (Nikon Corporation, Tokyo, Japan) and a 60 mm macro lens with a magnification of 1:10 and a distance of 80 cm. After transferring the images to the computer, the size of the wound in each image was measured and morphologically calculated using ImageJ software, version 1.45 (National Institutes of Health, Bethesda, Maryland, USA). Pathology samples were taken from 30 of the restored area. Histopathological slides were examined using Hematoxylin and Eosin (H&E) stains to evaluate and determine the extent of epithelialization, collagen filament arrangement, acute and chronic inflammatory cells, vascularization, and local fibroplasia. At the end of the study (30 days), rats were exterminated as standard using a high dose of Nesdonal. The collected data were analyzed by SPSS software, version 16 (IBM SPSS, Armonk, NY, USA). The central index of mean and scattering of standard deviation was used to describe the quantitative data. Data distribution and their normality were measured. To analyze the data in the study groups, Post hoc analysis of variance, ANOVA and Kruskal-Wallis tests were used, $p < 0.05$ was considered statistically significant (36). Isolation and culture of mesenchymal stem cells from Wharton's umbilical cord jelly: First, after obtaining and removing blood, the umbilical cord was immediately transferred to a cell culture laboratory in physiological serum containing antibiotic (penicillin / streptomycin 5%) and then washed with saline phosphate buffer (PBS) containing 1% amphotericin and 3% antibiotic. given. According to the methods mentioned in previous articles, cell isolation was performed (10), the umbilical cord was fragmented, blood vessels and fetal membranes were removed, and Wharton jelly was isolated and dissolved by tissue fragmentation. After isolation, the cells were transferred to a flask and cultured in an incubator at 37 ° C, 5% carbon dioxide and 95% moisture for several weeks until the third passage. The culture medium was changed every 3 days and the cells were examined daily under a microscope. The cells were then placed in a T25 flask (SPL, Korea) and in a DMEM culture medium (g I b co, USA) with 10% serum. FBS bovine embryos (GI bco, USA) and 1%

strepsin antibiotic (GI b co, USA) were kept until the third passage, followed by filling the flask with a density of over 80% using terpsin / EDTA (GI b co, USA, .25%) Passage and counted using a neobar slide and poured in equal numbers 160X1 in each microtype containing half (0.5) ml and subcutaneously using insulin syringe on the edges of fresh burn wounds Created injected (14) Animal studies and modeling of burns: In this study, which was performed on male Wistaran rats, 28 rats weighing 250-200 g were prepared from the animal house of Shahid Chamran University of Veterinary Medicine and after purchasing the animals, they were transferred to the animal house of the Faculty of Science and transferred to They were kept in standard conditions for a week to adapt to the new environment (access to water and food was unlimited and 12 hours of light and 12 hours of darkness). The boil was placed at 100 ° C and formed. First, the animals were anesthetized by intraperitoneal injection of a mixture of ketamine (80 mg / kg) and xylazine (10 mg / kg). The backs of the animals were shaved and disinfected with betadine. The hot stamp was placed on the body for 30 seconds. After induction of the burn model, rats were randomly divided into two groups of control and treatment. The rats of the control group were divided into three groups without using special treatment and the rats of the treatment group were divided into three groups: The second subcutaneous injection of stem cells around the burn area and the third group were treated with simultaneous cell injection and daily rubbing of the poultice. Animals were kept separately in standard cages with normal day and night conditions and unlimited access to water and food until the end of the treatment period (20, 21). For microscopic studies, the animals underwent chloroform facilitation on day 30 and the skin of the scalpel-treated area was dissected in 2x2 dimensions. After preparation of tissue sections and general staining of hematoxylin-eosin and specific Trichrome-Mason imaging, light microscopy was performed for histological examinations using I mage J software. Results using SPSS software (Ver.16) and ANOVA and T uke y statistical tests were evaluated as Mean ± SEM). The tables were drawn in Word 2016 and the graphs were drawn in Excel 2016 software and differences with $p < 0.05$ were considered significant. Research has also been done on the use of the amniotic membrane. According to this research, the amniotic membrane of the fetus can be stored in certain conditions after freezing and drying to be used free of microbial contamination. With this measure, the amniotic membrane of the fetus can be stored for one to two years. (28) And normal saline (80 m / l). Placental blood samples were sent to the laboratory for HBS-AG, HIVAB and HCVAB tests. After separation from the chorion and purification, the amniotic membrane was placed in normal saline solution containing gentamicin (80 mg / l) and stored at 4 ° C. In case of negative test results, amniotic fluid was used for patients' biological dressing (29). In some articles, the treatment of burns with vinegar can be seen. First, a clean cotton pad or a piece of sterile gauze was placed in vinegar and placed directly on the burn site. In order to have a greater effect, they used a thin towel in a

dilute vinegar solution as a soothing compress on the gas. [30] Or a sterile gauze was dipped in some of this essential oil and gently placed on the burned area of the skin to evaporate the essential oil to cool the burn and gradually heal. (30). There are people who say that if we put flour on the burn for ten minutes, it will not even blister, but this method has not been recognized yet and many people consider this method dangerous. (31)In other studies, potatoes were also a very effective treatment for burns. In this method, raw potatoes were first cut into thin slices and then placed on the burn and sliced. They had to rub the potatoes on the burnt part, but they did it carefully so that no pressure was applied to the burn and they waited for the juice to be released all over the burnt part. (32)

Results: Evaluation of Wharton Jelly Mesenchymal Stem Cell Morphology:Morphology of Wharton jelly mesenchymal stem cells cultured using an inverted microscope was performed. 1)) Histomorphometric results: Also, microscopic examination of samples with H&E staining on day 30 showed that the thickness of dermis and epidermis in treatment groups was significantly higher than the control group. Color changes in samples with Mason Trichrome staining showed that collagen synthesis in the samples of the treatment group started faster than the samples of the control group and the amount of collagen was higher. The intensity of the blue color of collagen, which indicates the amount of collagen formation, showed that the process of collagen formation in the treatment groups was clearly faster than the control group. The mean number of blood vessels and fibroblasts on day 40 after treatment showed a significant difference ($P < 0.05$) in the treatment and control groups. The morphological and histological results in this study showed that among a sample of treatment after 30 days In group samples that received only cells, wound healing and closure occurred faster than in samples that received only poultices (Figures 2 and 3). There was no significant difference between the number of blood vessels and the thickness of the epidermis in these two groups, but the comparison of the number of fibroblasts, collagen formation and the thickness of the dermis in the cell receiving group was significantly higher than the group receiving the dressing. Studies also showed that the simultaneous treatment group (dressing + cell) was repaired much faster than the other two groups and quantitative data from histological studies showed a significant increase in fibroblast cell count, angiogenesis and collagen formation and increased dermis thickness in The treatment group was simultaneous compared to the other two groups (Tables 1 and 2) Figure 1- Images obtained from morphological examination of human umbilical cord Wharton jelly mesenchymal stem cells Figure 1 - Images obtained from the morphology of human umbilical cord Wharton jelly mesenchymal stem cells. Images were recorded using an inverted microscope at 20% magnification. The red star refers to the exit of mesenchymal cells from tissue fragments. Figure 2. Morphological examination of dermis and epidermis of skin on day 30 using H&E staining

using light microscope. A * and A. control sample, and B. sample treatment with poultice, C * and C. cell therapy sample, D * D. (cell therapy + poultice) Row A images are taken with a magnification of 4 ˣ and row B images are taken with a magnification of 40 (. In this figure, blue stars represent the epidermis and orange stars represent the dermis. And black arrows indicate blood vessels. Figure 3 - Morphological study of collagen formation and density on day 30: Collagen density in the control group was significantly lower than the treatment groups. Collagen density was significantly higher in cell therapy + dressing group than in the two treatment groups. Collagen concentration was higher in the cell therapy group compared to the dressing group. A. control sample, B. poultice sample, C. cell therapy sample, D. cell therapy sample + poultice (images taken with 4ˣ magnification). In this figure, blue stars represent the epidermis and orange stars represent the dermis.

Conclusion: The results of the present study showed that subcutaneous injection of Wharton jelly mesenchymal stem cells in the burn area accelerated the wound healing process and reduced the time required for complete wound healing. The exact mechanism of action of stem cells in wound healing is not fully understood, although according to studies so far, the effect of various drugs and cell therapy together has accelerated wound healing (17). In general, the results of this study indicate that with the help of traditional medicine, a lot of valuable help has been given to the treatment of burns. For example, the substances mentioned above, such as vanilla essential oil, vinegar, potatoes, etc., although they help with burns, but the role of Wharton gel is more important. In the laboratory, the resulting cells were injected at the wound site and caused the wound to heal. In this study, the simultaneous use of coriander gum poultice and animal oil along with cell therapy had a significant effect on improving the healing process. It seems that the most important effect of coriander gum in improving the wound process can be due to its antimicrobial and anti-inflammatory properties. Also, although the mechanism of the effect of topical application of animal oil on wound healing is not clear, but it seems that the use of animal oils that contain large amounts of unsaturated fatty acids due to antimicrobial effects, reduce inflammation at the wound site and Acceleration of short-chain fat by providing essential fatty acids can increase cell proliferation in the skin and help form hypertrophic scars to repair skin damage and burns. In addition, scientific studies have reported that they inhibit the topical use of acids (22). Has been. In 2017, Bagheri et al. Used animal oil to treat a second-degree burn model in the burn model in Wistar rats and performed pathological and morphological studies on different days during the repair process. Contrary to expectations, however, their results showed that animal oil could not improve the fuel repair process, and they stated that this method did not improve the pathological monitoring criteria (24), although these differences could be due to differences in the type and quality of oil used. In the type of burn model creation and so on. The study also showed that concomitant use of coriander

gum with animal oil compared with control improved type 2 burn wounds in rats, but their comparison with silver sulfadiazine ointment showed that the effect of the ointment was significantly greater than the simultaneous use of gum. Coriander has been used with animal oil (20) In another study, Zohour et al. Stated that animal oil can have a positive effect on the healing process of burn wounds in rabbits (23) Comparing the average thickness of dermis and epidermis in treatment groups The control group was significantly higher. Studies by Marchin et al. (2012) showed that the repair of the epidermis is faster and the dermis is slow, and it takes about 3-4 weeks for my body to fully heal (23). Collagen fibers in tissue sections related to the group As shown in the results, collagen fibers in tissue sections belong to groups The treatments are network-like and wavy. Although the presence of collagen was observed in the control group, but this accumulation of collagen was localized and heterogeneous and no wavy and network arrangement of collagen fibers was seen. Also, fibroblast cells are the most effective cells in wound healing. These cells are involved in the formation of healthy tissue by increasing the number of damaged areas and the formation of a matrix of collagen fibers (25). Tetamanti et al. (2004) used fibroblast counting to determine wound quality and connective tissue formation in leech wound healing (25). Introduced surgical wound healing. (7) Our overall conclusion from the above studies is that Fibroblast count was used as an indicator in the evaluation of healing tissue. In addition, if a factor can stimulate and intensify the formation of new blood vessels at the right time and cause blood flow to the area. It can be said that the healing process is successful and the wound is prevented from deepening. Angiogenesis is essential for wound nutrition and oxygen supply. The effect of mesenchymal cells, especially through the production of angiogenesis factors, is a reason for stimulating the formation of the largest number of vessels on day 30 in cell-treated groups. In general, the results of this study showed that the simultaneous use of new methods of treatment, ie cell therapy with traditional methods can be appropriate and effective in improving the healing process of burns. Of course, to prepare a poultice for gum and oil, these two substances must be completely combined and combined with one hand, and it is recommended that the oil be sterilized if possible. Of course, in the continuation of the researchers' research, biological dressing had no effect on preventing the occurrence of thrombophlebitis in patients, and certainly traditional medicine has a special role in the treatment of burns. Conveniently and in the shortest time and at the lowest cost using the above-mentioned ingredients such as vanilla (in the treatment of minor burns), potatoes, vinegar and animal oil, etc. Deafness and appreciation to the good and patient teacher, Ms. abnoos, who provided the necessary instructions throughout the process.

Keywords: Cell Therapy, Burn, Stem Cells of the Wharton's Jelly, Coriander Tree Gum, Traditional Medicine

The evaluation of Trans chalcon on kidney injury induced by Gentamicintamicin in male Wistar rat (Research Paper)

Fatemeh Heidari,[1] Mahsa Ale Ebrahim,[2,*]

1. Department of Physiology, Faculty of Medicine, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran
2. Department of Physiology, Faculty of Medicine, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

Introduction: Kidney disease, which is becoming increasingly common, is one of the main public health problems. It is considered one of the 12 top causes of mortality worldwide, and the number of deaths from kidney disease increased by 18.4% from 2005 to 2019. Gentamicin is an antibiotic usually used to treat infections caused by Gram-negative bacteria. However, its long-term use may harm the kidneys. Trans-chalcone, a flavonoid precursor, has anti-inflammatory and antioxidant effects in addition to a broad spectrum of therapeutic properties including antioxidant, anticancer, antimicrobial, anti-ulcer and anti-inflammatory activities. Considering the beneficial effects of trans-chalcone, this research intended to evaluate its activity against gentamicin-induced kidney injury in male Wistar rats.

Methods: Forty-eight male Wistar rats were divided into 8 groups (n=6 per group): the control group (only food and water), three healthy experimental groups (trans-chalcone at 12, 24, or 50 mg/kg), the control group with kidney disease (gentamicin at 100 mg/kg) and three experimental groups with kidney disease (gentamicin at 100 mg/kg together with trans-chalcone at 12, 24, or 50 mg/kg). The period of treatment was 30 days for all groups, gentamicin was administered 8 times (twice-weekly) intraperitoneally and trans-chalcone once daily by intragastric gavage. At the end of the treatment period, the rats were anesthetized using combination of ketamine (90 mg/kg) and xylazine (10 mg/kg). Blood samples were taken from the heart and various biochemical factors including blood urea nitrogen (BUN) and serum creatinine, albumin and phosphate, sodium, potassium and calcium ions were measured. In addition, part of the kidney tissue was used for histopathological assessments and the rest was homogenized for evaluation of the activities of the antioxidant enzymes including catalase (CAT) and superoxide dismutase (SOD).

Results: In the control group with kidney disease (that received gentamicin) the levels of BUN and serum creatinine and the concentrations of phosphate, sodium and calcium ions increased significantly compared to the control (<0.001). Moreover, the activities of the antioxidant enzymes (CAT and SOD) decreased significantly compared to the control ($P<0.001$). Based on the findings of histopathological evaluation (in which H&E staining was used),

severe injury in kidney tissue in the form of acute necrosis of uriniferous tubules (50-75%) and strong penetration of mononuclear inflammatory cells (25-50%) was observed in the control group with kidney disease. No tissue injury or serum biochemical changes was recorded in the trans-chalcone control group compared to the control group. Furthermore, there was a dose-dependent improvement in biochemical and tissue results in the group receiving gentamicin together with trans-chalcone.

Conclusion: Trans-chalcone reduced toxic effects of gentamicin in kidney tissue probably by enhancing improvement in intracellular antioxidant status, removing free radicals, and exerting its anti-inflammatory property.

Keywords: Nephrotoxin, Kidney, Gentamicintamicin, Trans-chalcone, Rat

The frequecncy of Human Polyomavirus BK in colorectal cancer fecal samples (Research Paper)

Mahbube Farbarin,[1] Hoorieh Soleimanjahi,[2,*] Bita Bakhshi,[3] Zeynab Nasiri,[4] Kamal Fakhredini,[5]

1. Department of Virology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran.
2. Department of Virology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran.
3. Department of Bacteriology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran.
4. Department of Virology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran.
5. Department of Virology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran.

Introduction: Polomaviruses are oncogenic in rodent models and readily transform animal and human cells in-vitro. BKV is among this family of viruses. BK virus genome encodes a transforming protein known as Lareg T-Ag that intract with P53 and pRb tumor suppressor proteins altering cell cycle control and inducing malignant transformation. Thus there is a chance that BK virus could potentially promoting some neoplasia such as: colorectal cancer(CRC). CRC is the third most common cause of cancer death in the world. The risk factors developing CRC is associated with personal features such as age and gut microbiota. Many human neoplasms are often initiated by exposure to infectious agents.

Methods: Method: We assayed VP1 of BK virus in fecal samples, including 25 patients of CRC and 25 healthy cases. VP1 was detected by a PCR technique.

Results: Result: Based on our research, positive results in PCR, were obtained for 20% CRC group and just 4% sample in healthy group.

Conclusion: Conclusion: Taken together, PCR results for BK virus in patient samples idicate that may ye a causal relationship between the development of CRC and the virus existance. However the exact role of the BK virus is still controversial and needs to further study.

Keywords: Keywords: BK virus, Colorectal cancer, VP1, PCR, Gute microbiota.

The Functional Annotation and Gene Ontology Analysis of Caveolin-1 and Endomucin: The Downregulated Tumor-related Hub Genes
(Research Paper)

Arghavan Heydari,[1] Haniyeh Sadat Hosseininia,[2] Amin Ebrahimi Sadrabadi,[3,*]

1. Department of Microbiology, Kerman Branch, Islamic Azad University, Kerman, Iran
2. Department of Cellular and Molecular Biology, Faculty of Advanced Medical Science, Tehran Islamic Azad University of Medical Sciences, Tehran, Iran
3. Department of Stem Cells and Developmental Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACER, Tehran, Iran.

Introduction: Angiogenesis is the creation of new blood arteries from the arteries that play role in tumor development. Breast cancer is a common cancer in women and 58% of deaths associated with this type of cancer occurs in less developed countries. Despite significant improvement in early diagnosis, breast cancer death rates remain high yet. The study of molecular mechanisms of angiogenesis is necessary for developing new diagnostic and therapeutic strategies for breast cancer.

Methods: In order to more accurate analyze of correlation between angiogenesis and various pathways involved in the angiogenesis process, GEO dataset and ultimately selected 13 breast tumor and control samples has been used for analysis. BioJupies database has been used for in-depth analysis of a selected dataset.

Results: The downregulated genes in the breast cancer cells presented the differential expression which confirmed by volcano plot. Gene ontology (GO) analysis was performed on downregulated genes. The biological process (BP) analysis manifest the multiple biological roles for each gene. The cellular component (CC) analysis demonstrated the location where the protein/gene performs its molecular function.

Conclusion: This localization led us understand the correlation between the component of the plasma membrane and downregulation of specific genes which manages angiogenesis process. The protein-protein interaction (PPI) network of downregulated genes was constructed by STRING. It concluded that Caveolin-1 and Endomucin have the most significant correlation with other genes and their meaningful correlation with TEK and KDR is entirely obvious. The downregulation of selected genes on tumor cells led to expanding the angiogenesis process.

Keywords: Angiogenesis, Tumor-related Gene, Bioinformatics, GO Analysis, Breast Cancer

The hsa-miR-192-5p miRNA of the ABCG2 genes can be involved in the development of HCC by acting on the signaling pathways of Bile secretion. (Research Paper)

Zahra Khital,[1,*] Maryam Khital,[2] Mohammad Rezaei,[3] Mansoureh Azadeh,[4]

1. Zist Fanavari Novin Biotechnology Institute, Isfahan, Iran
2. Zist Fanavari Novin Biotechnology Institute, Isfahan, Iran
3. Zist Fanavari Novin Biotechnology Institute, Isfahan, Iran
4. Zist Fanavari Novin Biotechnology Institute, Isfahan, Iran

Introduction: Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer. HCC is the third leading cause of cancer-related death worldwide. Chronic hepatitis infection increases the risk of developing HCC. HBV increases HCC through direct and indirect mechanisms. The virus integrates its genome with the host and causes mutations in various cancer-related genes. Over the years, new molecular methods have been developed to better understand and detect cancer early. These molecular methods, such as DNA microarray and PCR-based array, can show us molecular markers for early detection and prognosis of cancer. Large-scale gene expression profiles provide important insights into the biology of liver cancer. The results of these methods identified signaling pathways that could serve as therapeutic targets.

Methods: Data were extracted from GEO and then analyzed by R studio. The method of data analysis was differential expression. Finally, three genes were selected and their target miRNAs were found through miRwalk3.0. Then, by analyzing the interactions and pathways, appropriate miRNAs were selected.

Results: GSE121248 on Gene expression profiling of chronic hepatitis B induced HCC and adjacent-normal tissues was used. One of the genes found in this assay is ABCG2, whose miRNA is hsa-miR-192-5p. hsa-miR-192-5p is a miRNA related to the ABCG2 gene. This miRNA is abundant in the liver and is also involved in bile secretion. Exogenous levels can contribute to the prognosis of chronic hepatitis. induces hepatic trans-differentiation from human umbilical cord Wharton's jelly derived mesenchymal stem cells. Another selected gene is GTSE1 and one of its miRNAs is hsa-4524b-3p. This gene and its miRNA are effective in HCC with negatively regulated p53 expression. High expression is associated with tumor size and is associated with the development of HCC and increased proliferation of cancer cells. The other selected gene is ITGA9 and its miRNA is hsa-miR-125b-3p. This gene is related to ECM-receptor interaction. Its expression is decreased in patients with HCC.

Conclusion: The ABCG2, GTSE1, and ITGA9 genes affect the progression of HCC disease by affecting Bile secretion, p53 signaling pathway, and ECM-receptor interaction in a ceRNA network.

Keywords: HCC , Hepatitis , microarray

The IGFBP-3 C-terminal IGF binding domains (Review)

Nima Naseri,[1,*]

1. Department of Clinical Biochemistry, Hamadan University of Medical Science, Hamadan, Iran

Introduction: IGFBP-3 is a member of the six binding protein family, which is known to be the major carrier of insulin-like growth factors 1 and 2 in serum. Through its N and C-terminal domains, IGFBP-3 involves binding to insulin-like growth factors and regulating the function of insulin-like growth factors in cell proliferation and differentiation, and regulates their function and bioavailability that is associated with the pathophysiology of several illnesses like Cancers and Diabetes. In the IGFBP-3 structure, certain amino acid domains and sequences are involved in binding to IGFs, which are highly conserved among the IGFBPs family. A recent study in 2020 showed that IGFBP-3 C- terminal domain-derived peptides in both Wild and Mutant forms, with significant potency similar to IGFBP-3, were able to bind to hyaluronans and like domain-derived peptides, binds to metalloproteinases. Therefore, by binding to extracellular matrix components such as heparin, hyaluronan, and proteases, this peptide prevents the binding of IGFBP-3 to the extracellular matrix, increases the free form of IGFBP-3, and the resistance of this protein to proteases.

Methods: The different articles associated with IGFBP-3 C-terminal peptide were searched and collected base on Mesh word advanced search in Pubmed.

Results: A recent study in 2020 showed that IGFBP-3 C- terminal domain-derived peptides in both Wild and Mutant forms, with significant potency similar to IGFBP-3, were able to bind to hyaluronans and like domain-derived peptides, binds to metalloproteinases.

Conclusion: Therefore, by binding to extracellular matrix components such as heparin, hyaluronan, and proteases, this peptide prevents the binding of IGFBP-3 to the extracellular matrix, increases the free form of IGFBP-3, and the resistance of this protein to proteases.

Keywords: IGFBP-3, IGFs, Cancer, Diabetes

The Impact of MiR-200c in Cervical Cancer Chemoresistance (Review)

Farzaneh Karimi,[1,*] Kazem Dastjerdi ,[2]

1. Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran
2. Department of Medical Biotechnology, Faculty of Medicine, Birjand University of Medical Sciences, Birjand, Iran

Introduction: Cervical cancer is a common gynecological cancer-related death among women worldwide. Although chemotherapy is an effective treatment for this cancer, resistance to anti-cancer therapy is still considered a major problem that leads to relapse and mortality. A better understanding of drug resistance mechanisms is essential to promote the efficacy of cancer therapeutic strategies. One of the critical leading causes of chemoresistance is the evasion of apoptosis. Activation of caspases as a pivotal step in the induction of apoptosis has two main pathways including extrinsic pathway controlled by tumor necrosis factor (TNF) receptor family and intrinsic apoptotic pathway regulated by B-cell lymphoma 2 (BCL2) family. Accumulating evidence has indicated that in various cancers chemoresistance might be due to the alteration in microRNAs (miRNAs). Therefore, miRNAs dysregulation might control anti-cancer drug resistance. MiR-200c is one of the important miRNAs involved in cervical cancer and can be a novel candidate target for therapeutic methods.

Methods: Several studies have demonstrated that miR-200c plays a considerable role in different types of cancers. In these studies, usually quantitative reverse transcription polymerase chain reaction (qRT-PCR) and real-time PCR were used for investigating the miRNA expression level between resistant and sensitive cancer cell lines. Moreover, to evaluate the chemoresistance characteristics in cancer cells, MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay was used. Western blot and apoptosis assay were also used to reveal the drug resistance mechanisms of miRNA.

Results: Zhu et al. indicated that miR-200c was downregulated while BCL2 was upregulated in gastric and lung cancer cell lines. On the other hand, overexpression of miR-200c sensitized cells to anti-cancer drugs such as vincristine. Therefore, enforced miR-200c expression can reduce BCL2 protein level and sensitize tumor cells to vincristine by inducing apoptosis.

Conclusion: In this review, we propose that upregulation of miR-200c that can sensitize gastric and lung cancer cells to vincristine can also be

investigated in cervical cancer cells and provide valuable miRNA-based therapeutic methods to overcome chemoresistance in this cancer.

Keywords: Cervical cancer, Chemoresistance, MiR-200c

The importance and role of cancer stem cells in cancer treatment (Review)

Fatemehsadat Hoseini,[1,*]

1. Student research Center, Baharestan 1 Education Office, Baharestan 1, Tehran, Iran

Introduction: Cancer stem cells are cancer cells that are found in tumors or blood-related cancers and have characteristics similar to normal stem cells (especially in their ability to become all types of cells). In order to identify the characteristics of cancer stem cells, they must be isolated from the entire cell population. These cells have specific markers on their surface that distinguish them from other cells. These markers are specific antigens and receptors and can be one of the best diagnostic methods for isolating these cells in different tumors. Such cells appear to be conserved as a separate population within the tumor and then grow to metastasize to form a new tumor; Therefore, the development of therapies in which cancer stem cells are targeted is very promising for cancer patients, especially those with metastases.

Methods: Cancer stem cells are unevenly distributed within tumor tissue and, like natural stem cells, have the ability to self-regenerate and are responsible for tumor survival and differences in its genetic and metabolic characteristics. These cells are preserved in patients undergoing chemotherapy and, by unequal division, cause the formation of new tumor cells with multiple resistance characteristics. There are two ways to use cancer stem cells to treat cancer: to differentiate cancer stem cells and to use cancer stem cells as carriers of carcinogenic viruses. In the treatment of differentiation induction, substances are used that induce the differentiation of cancer stem cells. This method is based on the idea that cancer stem cells are cells that are in an undifferentiated state and multiply uncontrollably and rapidly. Although differential treatment does not kill cancer stem cells, it limits their growth and regeneration and ultimately allows the removal of malignant cells using traditional therapies (such as chemotherapy).Carcinogenic viruses are natural or genetically modified species that kill cancer cells in a programmed and selective manner. Stem cells are one of the most important cellular carriers for the treatment of carcinogenic viruses. The carrier cell tends to accept the virus.

Results: It is thought that if cancer stem cells can be eradicated, they will be completely successful in treating cancer. Therefore, specifying methods for diagnosing these cells improves patients' chances of survival by reducing tumor recurrence.

Conclusion: The future challenge in treatment should include increasing the efficiency of targeting cancer stem cells in tumors. It is hoped that future studies can make further progress in this area.

Keywords: Cancer, Cancer Stem Cell

The importance of nutrition education in old age and related disease prevention (Review)

zeinab sadat moosavi fard,[1,*]

1. Department of Nursing, faculty of nursing, Bandar Abbas Branch, Islamic Azad University, Bandar Abbas, Iran.

Introduction: In recent years, the role of nutrition in controlling risk factors and preventing nutritional deficiencies that occur in old age has received more attention. According to the definitions provided, it refers to people aged 65 and over. Today, there are 600 million seniors over the age of 60 worldwide. And it is predicted to reach two billion people in 2025. According to the last census of 1390 in the country, there are 6159676 elderly people in the country, which constitute 1.8% of the total population. Healthy eating as an essential element of health in this age group needs special attention and improving nutrition can greatly prevent these problems, so one of the important issues in this regard is to increase the awareness and attitude of the elderly. Therefore, the purpose of this review is to evaluate the effect of nutrition education in the elderly.

Methods: Searching databases of Pubmed, Science direct, Google scholar, Side, Iranmedex, Scopus and using the keyword nutrition, the elderly, prevention, articles published in Persian and English were collected until August 2015. The obtained articles were reviewed based on the title, abstract of the article and their full text and all the indicators were examined. A total of 45 articles related to the purpose of this study remained for systematic review.

Results: Aging is thought to lead to increased oxidative stress and imbalance between the formation and destruction of free radicals, and thus can affect the composition of blood lipids, and inactivity is a feature of old age. As a result of all these factors, it causes chronic diseases such as cardiovascular disease, diabetes, and high blood pressure. Therefore, proper nutrition is the main condition for the survival of the elderly. Nutrition education is very important in this regard.

Conclusion: Decreased physical fitness of the elderly due to old age limits the possibility of access to all the nutrients needed by the elderly, while isolation and loneliness cause mental problems and reduce appetite and motivation to eat. Therefore, measures should be taken to support the improvement of nutritional status and their loneliness. Due to the worrying malnutrition of the elderly, nurses can play an important role in nutrition-based education.

Keywords: nutrition, education, old age, disease prevention

The importance of the impact of the economic record on the structure of the health system (Review)

Parisa Mehrasaniya ,[1,*]

1. University of Applied Sciences

Introduction: In this article, we first define economics and how it arises, and then discuss health economics, and the application of each in the health system and the economic records that affect health communities. And as a result, the impact of the questions that prevent the economic record in health and wellness, which must be answered by the country's economic system as well as the country's health system

Methods: In this article, studies have been done based on numerous articles and field books in this field.

Results: The basic premise of health economics is that health system societies must answer these three fundamental questions in economics: What services should be provided? How services are produced or provided. For whom it is produced or presented; The country's economic system must answer these questions. It depends on the country's policy and that these questions have special problems in the field of health and are not answered properly.

Conclusion: That we must study and analyze the economy in developing countries to prevent the record of the economy in the field of health and also the inflation of the structure, the health system. Because in the current situation, developed countries control and monitor this issue and adopt policies and plans, and they are reviewing.

Keywords: Economics, Health ,Management, Record

The importance of vitamin C, vitamin E, and B-carotene, as "antioxidant micronutrients", in boosting immunity via reducing inflammation and oxidative stress for the prevention and treatment of COVID-19 (Review)

Davood Jafari,[1,*] Melika Noori,[2]

1. 1. Department of Immunology, School of Medicine, Zanjan University of Medical Sciences 2. Immunogenetics Research Network (IgReN), Universal Scientific Education and Research Network (USERN)
2. 3. Student of Surgical technology, School of Nursing and Midwifery, Zanjan University of Medical Sciences 2. Immunogenetics Research Network (IgReN), Universal Scientific Education and Research Network (USERN)

Introduction: The immune system recognizes foreign invaders and protects the body from pathogens. This system can be affected by many environmental and genetic factors. Oxidant-antioxidant balance is one of these factors which is required for the proper function of the immune system. Oxidative stress is observed in the case of the imbalance between the production of reactive oxygen species and antioxidant defenses. Exceed free radicals may impair crucial biomolecules and regulatory pathways involved in inflammation, which can affect the cells of a variety of tissues. Hyperinflammation, caused by an uncontrolled reaction to immune-related stimuli, is supposed to be associated with incidence and symptoms' intensity of COVID-19 infection. The goal of this study is to highlight some new findings on the impact of vitamins C, E, and β-Carotene on the prevention and treatment of SARA-CoV-2 by modulating oxidative stress and inflammation.

Methods: The available literature in the 'PubMed,' 'Google Scholar' and 'Science Direct' databases were analyzed using the keywords including nutrients, immune system, COVID-19, oxidative stress, inflammation, and the results with scientific evidence for the positive effects of vitamins C, E, and β-Carotene on inflammation, oxidative stress, and the function of the immune system during the infection were summarized.

Results: Recent evidence reveal that several transcription factors including NF-κB, AP-1, p53, HIF-1α, β-catenin/Wnt, and Nrf2 can be activated by oxidative stress. These transcription factors modulate the gene expression of a variety of inflammation-induced factors including activating and inhibitory receptors, inflammatory chemokines, and cytokines, and dysregulation of this loop can impair the function of immune system and intensify the COVID-19 disease condition. It has been demonstrated that pertinent intake of antioxidant nutrients can help to boost the immune system by decreasing excessive inflammation and oxidative stress.

Conclusion: It is indicated that some antioxidant micronutrients such as vitamin C, vitamin E, and β-Carotene have key roles in strengthening the immune system, thereby helping the prevention and treatment of COVID-19 disease.

Keywords: Vitamin C, vitamin E, β-carotene, COVID-19, oxidative stress

The importance of vitamin D on health and the need for mass production (Review)

Mana Kiani,[1,*] Mojtaba Mortazavi,[2]

1. Department of Biotechnology , institute of science and high technology and Environmental Sciences , Graduate university of advanced technology , Kerman , Iran .
2. Department of Biotechnology , institute of science and high technology and Environmental Sciences , Graduate university of advanced technology , Kerman , Iran .

Introduction: Vitamin D is a fat-soluble steroid that acts as a pre-hormonal in the body and regulates blood calcium and phosphate. It is also an anti-rickets vitamin that prevents many diseases in the body. Vitamin D is naturally produced in skin cells under the sun's ultraviolet rays and then becomes active in the liver and kidneys. Vitamin D can also be obtained from foods such as meat and fish liver and some kinds of mushrooms. Vitamin D has several forms, the two most well-known of which are D3 and D2, both of them can be absorbed in the gut.

Methods: Methods: In this study, several methods of vitamin D production were investigated. In the first method, the chemical production of vitamin D was investigated using lanoline extracted from sheep`s wool. In the second method, the use of probiotic bacteria to transfer vitamin D to the intestine and in the third method, the production of vitamin D using shiitake mushrooms treated with ultraviolet lamps was studied.

Results: The results of this study show that vitamin D deficiency has been observed in different parts of the world and always affects people's health. Also, various factors such as skin color and the direction of sunlight in any geographical area can affect the production of vitamin D in the body. In addition, several factors such as skin color and the direction of sunlight in any geographical area can affect the production of vitamin D in the body. But one of the most important issues is the way people use to wear clothes, which is more pronounced in Muslim-majority countries, in these country people cover most of the body surface and minimize the amount of sunlight received by skin cells (Especially in women).

Conclusion: Adequate amounts of vitamin D in the blood can prevent many diseases and abnormalities such as obesity, type 2 diabetes, preeclampsia, periodontitis, cancer death, etc., but many groups of people around the world for some reasons such as low sunlight in the living area they do, Excessive coverage or other items mentioned, producing insufficient amounts of vitamin

D is not naturally possible in skin cells. Therefore, the importance of taking vitamin D orally can be seen here. It should be noted that in addition to foods that have different levels of vitamin D, tablets and capsules containing vitamin D are also a good way to compensate for the lack of this vitamin in the body.

Keywords: Keywords: Vitamin D , Steroid , lanolin

The influence of interferon-γ on cardiac and renal histopathological changes induced by carbamazepine (Research Paper)

azam soleimani,[1,*] soghra bahmanpour,[2] fatemeh karimi,[3]

1. Shiraz University of Medical Sciences, Shiraz, Iran
2. Shiraz University of Medical Sciences, Shiraz, Iran
3. Shiraz University of Medical Sciences, Shiraz, Iran

Introduction: Epilepsy is one of the common nervous system disorders affecting about 0.3–0.7 % of pregnancies. Children born to mothers with epilepsy are at increased risk for low birth weight, prematurity, neonatal death, congenital malformations. On the other hand, women with epilepsy must use antiepileptic drugs (AEDs) during pregnancy. AEDs (e.g. valproic acid, carbamazepine and diazepam) may affect the fetal development during pregnancy. Carbamazepine (CBZ) is one of the oldest AEDs applied worldwide. There are many researches to show that CBZ is a teratogen. Children of mothers with epilepsy which used CBZ during pregnancy showed an increased rate of congenital abnormalities such as cardiovascular and urinary tract anomalies, NTDs, cognitive failure and cleft palate. There have been various studies indicating the effectiveness of maternal immune stimulation (MIS) in preventing the birth defects. The first goal of this study was to assess the histological teratogenic effects of CBZ during pregnancy. The second aim was to evaluate the possible protective effect of IFN-γ on the histopathological changes in the fetal heart and kidney following exposure to CBZ.

Methods: Tissue preparation The fetuses were delivered by hysterectomy on the 18th day of gestation. Five fetuses were selected randomly from each group. The body weight and crown-rump length (CRL) of each fetus were recorded. The hearts and kidneys were removed, processed, sectioned (25 µm), and stained by hematoxylin and eosin (H&E).

Results: The results showed that the body weight as well as heart and kidney weights decreased in the CBZ-treated group in comparison with the control group. It also showed a significant decrease in crown-rump length of the CBZ group when compared with the control group. However, after stimulation of the maternal immune system of CBZ-treated with INF-γ, this substance significantly prevented these parameters changes ($p < 0.05$) Volume of the heart and ventricles The total volume of the heart and left ventricle were reduced in the CBZ-treated group as compared to the control and INF-γ groups ($p < 0.05$). The decreased total volume of the heart in CBZ group was however restored by INF-γ treatment ($p < 0.05$). Volume of the kidney, cortex and medulla The total volume of the kidney, renal cortex and medulla was reduced in the CBZ-treated group in comparison to the control and INF-γ

groups ($p < 0.01$). Yet, the treatment of CBZ treated group with INF-γ protected the loss of the total volume of the kidney and medulla ($p < 0.05$). Heart histopathological evaluation Examination of the fetal cardiac sections in the control and INF-γ groups showed normal histological structure of the myocardium. The most alterations were observed in the CBZ group. This group showed loss of normal tissue appearance with degeneration of the cardiomyocyte and hyperemic blood vessels. However, treatment of CBZ group with Interferon-γ resulted in reduction of the damage. The score of cardiac tissue damage was significant in the CBZ group when compared with the other groups ($p < 0.01$). Kidney histopathological evaluation Examination of the fetal kidney sections in the control and INF-γ groups showed normal renal structure. However, the CBZ group showed degeneration of the proximal and distal tubules with enlarged urinary space and inflammatory infiltrate cells in the CBZ group. On the other hand, these alternations were less significant in the CBZ + INF-γ group. The score of the renal tissue damage was significantly higher in the CBZ group when compared with the other groups ($p < 0.01$).

Conclusion: The present research attempted to study the effect of CBZ and IFN-γ use during pregnancy on quantitative and histopathological changes of the fetal vital organs. The first part of the current study showed that CBZ used in pregnant mice reduced the CRL and body weight as well as fetal heart and kidney weights. These results are consistent with pervious researches that showed CBZ can lead to intrauterine growth retardation which is manifested by low body weight and length reduction. The findings of the second part of the present research indicated a reduction in the volume of the fetal heart and kidney following CBZ. This is consistent with our histopathological findings. The current findings revealed that IFN-γ could protect against the adverse effects of CBZ on histopathological changes of the fetal tissues.

Keywords: carbamazepine, interferon-γ, heart, kidney, mice

The Interplay Between Mast Cell and Influenza Virus (Review)

Hassan Karami,[1,*]

1. Department of Virology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

Introduction: Mast cell (MC) is a granule-containing tissue sentinel cell with a key role in immediate anti-viral innate immunity. This cell is abundant and protective in airway responding pathogenic respiratory viruses like Influenza viruses within minutes. Here, we will explore the relationship between MCs and the Influenza virus discussing the role of these cells in the pathogenesis of the virus infection.

Methods: For the present study, we reviewed three scientific databases including PubMed, Google Scholar, and Science Direct with the following keywords “Influenza virus” and “mast cell” without a time limit to find the most relevant studies in line with our purpose.

Results: In humans, MCs are well infected with the Influenza virus through an engagement of the expressed pattern-recognition receptors (PRRs), however, this infection is abortive in type and has a limitation in viral replication. Directly, the Influenza virus can activate MCs. Dynamically, this activation is a virus-to-cell signal-dependent resulting in an excessive immunity against the virus. This can also be mediated by MC-derived mediators such as tryptase, histamine, cytokine, and chemokines with profound biological effects. These molecules lead to immune cell maturation, recruitment, and activation as well as pulmonary inflammation. Moreover, accumulating mast cell progenitors has also been found in the site of infection following the release of the mediators. Collectively, these events resulting in immunopathological lesions left in the lower respiratory tract. Upon infection with Influenza virus, the population of MCs in pulmonary tissue and the levels of histamine metabolites via calcium-dependent exocytosis pathway showing an increasing trend suggesting a possible role and a positive correlation for MCs in the process of inflammation which is observed during the infection of Influenza virus. MCs are also prone to cell death through the activation of the classical intrinsic pathway independent of MC activation.

Conclusion: MCs are important as they contribute to Influenza virus immunopathology. These cells can determine the course of infection and they can enhance the virus-mediated disease. Further studies are needed to find how MCs interact with respiratory viruses like the Influenza virus in a virus-cell interaction.

Keywords: Influenza Virus, Mast Cell, Inflammation

The need to identify new diagnostic methods for resistant Acinetobacter baumannii isolates (Review)

Zahra Mottaghiyan,[1] Davoud Esmaeili,[2,*] Mohammad Niakan,[3]

1. Department of Microbiology, Faculty of Medicine, Shahed University, Tehran, Iran
2. Department of Microbiology and Applied Microbiology Research Center, Systems Biology and Poisonings Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran
3. Department of Microbiology, Faculty of Medicine, Shahed University, Tehran, Iran

Introduction: Acinetobacter baumannii is a gram-negative and lactose-negative bacterium Which is increasingly regarded as an important cause of infections Hospitals such as ventilator-associated pneumonia Secondary meningitis, surgery site infections and Urine infections especially in patients admitted to intensive care.Treatment of Acinetobacter baumannii infections often with phenotypes Multidrug resistant, such as resistance to broad-spectrum beta-lactams, Aminoglycosides and fluoroquinolones become difficult. According to the World Health Organization, the most important bacterium that threatens human life is Acetobacter baumannii resistant to carbapenem. Therefore, one of the prominent bacteria with multidrug resistance is Acinetobacter baumannii and it is also one of the worrying resistances is ESBL and MBL. Due to the increasing prevalence of available strains in recent years, so the identification of new molecular methods in the rapid and correct diagnosis of these strains and the select of immediate and appropriate treatment of patients seems necessary.

Methods: In this study, to access the articles, search the PabMed and Google Scholar databases using keywords such as "new methods:", "resistant acinetobacter baumanii isolates" or phrases such as "new methods identify resistant acinetobacter baumanii isolates". The articles were reviewed in two separate sections outside Iran and inside Iran.

Results: In the articles found, researchers used molecular techniques such as PCR and Multiplex PCR search the presence of ESBL genes such as TEM, CTX-M, SHV and MBL genes include IMP, VIM, GIM and NDM in Acinetobacter baumannii isolates.

Conclusion: The results indicate that the identification of new diagnostic techniques such as advantages in addition to faster and better detection of Acinetobacter baumannii isolates resistant to multidrugs and immediate and appropriate treatment of nosocomial infections, increase readiness for

diagnosis, especially during epidemics. And reduce the cost of personal care and health.

Keywords: Acinetobacter baumanii, Multiplex PCR, ESBL, MBL

The Nuclear Factor Kappa B (NF-kB) signaling in cancer development and immune diseases (Review)

Mohammad Reza Zinatizadeh,[1,*] Bettina Schock,[2] Ghanbar Mahmoodi Chalbatani,[3] Peyman Kheirandish Zarandi,[4] Seyed Amir Jalali,[5] Seyed Rouhollah Miri,[6]

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Introduction: The nuclear factor kappa B (NF-kB) family of transcription factors plays an essential role as stressors in the cellular environment, and controls the expression of important regulatory genes such as immunity, inflammation, death, and cell proliferation. NF-kB protein is located in the cytoplasm, and can be activated by various cellular stimuli. There are two pathways for NF-kB activation, as the canonical and non-canonical pathways, which require complex molecular interactions with adapter proteins and phosphorylation and ubiquitinase enzymes. Accordingly, this increases NF-kB translocation in the nucleus and regulates gene expression. In this study, the concepts that emerge in different cellular systems allow the design of NF-kB function in humans. This would not only allow the development for rare diseases associated with NF-kB, but would also be used as a source of useful information to eliminate widespread consequences such as cancer or inflammatory/immune diseases.

Methods: The nuclear factor kappa B (NF-kB) family of transcription factors plays an essential role as stressors in the cellular environment, and controls the expression of important regulatory genes such as immunity, inflammation, death, and cell proliferation. NF-kB protein is located in the cytoplasm, and can be activated by various cellular stimuli. There are two pathways for NF-kB activation, as the canonical and non-canonical pathways, which require complex molecular interactions with adapter proteins and phosphorylation and ubiquitinase enzymes. Accordingly, this increases NF-kB translocation in the nucleus and regulates gene expression. In this study, the concepts that emerge in different cellular systems allow the design of NF-kB function in humans. This would not only allow the development for rare diseases associated with NF-kB, but would also be used as a source of useful information to eliminate widespread consequences such as cancer or inflammatory/immune diseases.

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Conclusion: The nuclear factor kappa B (NF-kB) family of transcription factors plays an essential role as stressors in the cellular environment, and controls the expression of important regulatory genes such as immunity, inflammation, death, and cell proliferation. NF-kB protein is located in the cytoplasm, and can be activated by various cellular stimuli. There are two pathways for NF-kB activation, as the canonical and non-canonical pathways, which require complex molecular interactions with adapter proteins and phosphorylation and ubiquitinase enzymes. Accordingly, this increases NF-kB translocation in the nucleus and regulates gene expression. In this study, the concepts that emerge in different cellular systems allow the design of NF-kB function in humans. This would not only allow the development for rare diseases associated with NF-kB, but would also be used as a source of useful information to eliminate widespread consequences such as cancer or inflammatory/immune diseases.

Keywords: Cancer, Immunity, Inflammation, NF-κB, Signaling

The pattern of Endothelial Microparticles following intervention with Paleolithic-based low-carbohydrate vs. moderate carbohydrate diets in adults with metabolic syndrome (Research Paper)

Farnoosh Shemirani,[1] Kurosh Djafarian,[2] Akbar Fotouhi,[3] Leila Azadbakht,[4] Nima Rezaei,[5] Maryam Mahmoudi,[6,*]

1. Tehran University of Medical Sciences
2. Tehran University of Medical Sciences
3. Tehran University of Medical Sciences
4. Tehran University of Medical Sciences
5. Tehran University of Medical Sciences
6. Tehran University of Medical Sciences

Introduction: Several recent studies have been undertaken into carbohydrate-restricted diets. it has not been clearly demonstrated whether diets with different proportions of energy from carbohydrate exert distinct effects on endothelial damage or not. The current randomized clinical trial (RCT) has been conducted to further elucidate the effects of severe and mild carbohydrate restriction on endothelial integrity in adults with metabolic syndrome (MetS).

Methods: Eighty adults with metabolic syndrome were randomized to one of the four carbohydrate restricted diets: Paleolithic-based low-carbohydrate diet with calorie-counting method (PLCD-CC) (n=20), Paleolithic-based low-carbohydrate diet with fixed-diet planning method (PLCD-Fixed) (n=20), moderate-carbohydrate diet with calorie-counting method (MCD-CC) (n=20) and moderate-carbohydrate diet with fixed-diet planning method (MCD-Fixed) (n=20) for 10 weeks. PLCD is defined as a diet consisting of 25-30% of energy from carbohydrate, 30% of energy from protein and 40-45% of energy from fat and encourages consumption of fruits, vegetables and lean meat. MCD is characterized as 40-45% carbohydrate, 30% protein and 30-35% fat. Appetite-regulatory hormones and plasma level of endothelial microparticles were assessed at baseline and at the end of 10 weeks.

Results: A total of 69 participants aged 42.95 (9.27) with metabolic syndrome completed the trial. At the end of current 10-week dietary intervention trial, we found significant reduction in CD 144+/42b-/31- EMPs in PLCD-Fixed intervention group ($p<0.05$). Mean changes of CD 144+/42b-/31- EMPs was also marginally statistically significant between 4 intervention groups ($p=0.073$). The within-group changes in ghrelin was significant in all 4 groups ($p<0.05$). However, despite clinical significance, the within- and between-group change in PYY was not statistically significant at the end of trial.

Conclusion: The current RCT in adults with metabolic syndrome revealed that both moderate and Paleolithic-based low carbohydrate diets with both delivery approaches have comparable beneficial effects in terms of appetite regulation and endothelial integrity.

Keywords: Carbohydrate restriction; Paleolithic Diet; Appetite; Endothelial Microparticles

The Perspective of Dysregulated Urinary Exosomal RNAs in Diagnosis of Prostate cancer: A Systematic Review (Review)

Fatemeh Davari,[1,*] Ayda Ghorbani,[2] Parisa Badameh,[3] Mina Younesi,[4] Mahsa Maleki,[5]

1. Tarbiat Modares university
2. Tarbiat Modares university
3. Tarbiat Modares university
4. Tarbiat Modares university
5. Tarbiat Modares university

Introduction: Prostate cancer (PCa) is the second cause of cancer death in men worldwide. Current treatments are not effective enough, as there is a challenge in the clinical management of PCa is the inefficiency of present methods for early detection of PCa, such as quantitative serum PSA testing and Digital Rectal Examination DRE. Quantitative determination of PSA is inappropriate in indolent forms of PCa, does not have sufficient sensitivity and specificity to identify and classify cancers at lower stages, and usually does not eliminate the need for biopsy or repeat of the biopsy, which causes the patient anxiety. Typically, 70% of PCa cases did not diagnose at initial biopsy because of false-negative or tumor heterogeneity. DRE also has side effects such as infection with antibiotic-resistant pathogenic bacteria and the risk of rectal damage and rupture. Recently exosomes have been used in the diagnosis of solid tumors and targeted drug delivery. Exosomes contain proteins, lipids, DNAs, mRNAs, and non-coding RNAs found in body fluids such as serum, plasma, saliva, cerebrospinal fluid, milk, semen, and urine. Also, the unique properties of exosomes like non-invasiveness, stability, biocompatibility, permeability, low toxicity, small size(50-150 nm), low immunogenicity, and their significant amount in body fluids make them suitable carriers of potential biomarkers for prostate cancer diagnosis. Examining the expression changes of non-coding RNAs, especially MicroRNAs, due to their high sensitivity and specificity in urinary exosomes (ExomiRs) between PCa patients and the control group can be a prominent step in non-invasive and early detection of PCa.

Methods: Search for the keywords Biomarker, Prostate cancer, Diagnosis, MicroRNA, Urinary exosomes, and Non-invasive in PubMed and Google scholar databases had more than 800 articles in the last two years. Fifty studies in recent years with the most relevant to the purpose of this study, which received the highest citations and in ISI journals. Inclusion criteria: Studies with urine biopsy, at least 50 patients, exosome extraction. Exclusion criteria: Studies on semen, blood or solid tissue and low density groups.

Results: EPI test with PCR examined the expression PCA3 (LncRNA), a family of ERG mRNAs (including TMPRSS2) and SPDEF in urinary exosomes are showed that these biomarkers prevent up to 30% of unnecessary primary and secondary biopsies in people with PSA 2- 10 and identified individuals with HGPCa grade (Gleason score 7 or higher) in this range of PSA and offers a new more accurate classification of PCa. Overexpression of these mRNA; ITSN1, ANXA3, and SLC45A3 from a seven-panel was more significant than the ten, five, and four-panel mRNA in prostate cancer diagnosis. miR-375-3p and miR-574-3p were introduced as more efficient (due to hybrid formation). Multivariable research of 7 mRNA panel, 2 microRNA panel, PCA3 value, age, serum PSA, prostate volume, and DRE result was evaluated with P-value 2.27 × 10^-82 and introduced as a PCa detection tool. Evaluation of increase in urinary exomiRs by lectin induced aggregation method miR-21-5p, miR-141-5p and miR-574-3p and decrease in HSA-miR-21-5p, HSA-miR-326, HSA-miR-375, HSA-miR-574-3p, HSA-miR-2110, besides measurement of miR-196a-5p, miR-501-3p, miR-19, miR-145 and miR-2909 by deep sequencing and then confirmation by PCR, miR-196a-5p, miR-501-3p, miR-451a, miR-486-3p, miR-486-5p, miR-532-5p, miR-26a-5p, miR-99b-3p ,and circ_0044516 by NGS and then rt-qPCR, which are upregulated in PCa, and also check the level of miR-21, miR-204, miR-375, miR-125, miR-1290, miR-572, miR-143-3p, miR-92-a1-5p, miR125-b,miR-107, miR-34a, miR-483-5p and lncRNA panel (MALAT1 + PCAT-1 + SPRY4-IT1) are suitable diagnostic biomarkers for prostate cancer. It seems that detection of two urinary exomiRs HSA-miR-6090 and HSA-miR-3665 in PCa and normal groups compared by hydrogel-based hybridization chain reaction(HCR) are a robust diagnostic approach in PCa. MiR-30b-3p and miR-126-3p were validated by the Microarray method in diagnosis of prostate cancer.

Conclusion: Early detection of PCa by urinary exomiRs has so far helped more than 50,000 patients, but the current information is still insufficient for widespread clinical use, until more advancement of personalized medicine and more efficient and independent panels.

Keywords: Exosomes, Diagnosis, Prostate cancer

The prevalence of Virulence Factors of Streptococcus Pyogenes Isolated from Pharyngitis and Septicemia in Bushehr (Research Paper)

Somayyeh Gharibi,[1,*] Mahnaz Gholipour shahrak,[2] Askar Rezai Darvishi,[3] Abbas Yadegar,[4] Saeed Tajbakhsh,[5] Zeinab Asen,[6]

1. Department of Microbiology, School of Sciences, Kherad Institute of Higher Education, Bushehr, Iran
2. Department of Microbiology, School of Sciences, Kherad Institute of Higher Education, Bushehr, Iran
3. Department of Microbiology, School of Sciences, Kherad Institute of Higher Education, Bushehr, Iran
4. Foodborne and Waterborne Diseases Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
5. Department of Microbiology and Parasitology, School of Medicine, Bushehr University of Medical Sciences, Bushehr, Iran
6. Department of Microbiology, School of Sciences, Kherad Institute of Higher Education, Bushehr, Iran

Introduction: Streptococcus pyogenes, GAS, is the cause of skin, invasive and immune system disease. Pharyngitis and septicemia are the most common and severe diseases caused by this bacteria, respectively. Different virulence genes are involved in the onset, severity and survival of infection, which are expressed in different strains. This study investigated the presence of some virulence genes in samples isolated from patients with pharyngitis and septicemia.

Methods: This study was performed on 16 isolates isolated from patients with pharyngitis and 2 isolated from the sample of septic patients. After culturing and purifying the bacterial strain, DNA of each bacterial strain was extracted. They were confirmed by a housekeeping gene primer, Spy 1258 by PCR and then the presence of virulence genes such as scpA, speB, speG, hasA, spd3, sla and silC was examined.

Results: The presence of spy1258 gene was confirmed in all strains (100%). The S. pyogenes ATCC19615 contained all of 5 genes (speB, speG, scpA, hasA and spd3). Four samples (22.2%) carried the scpA gene and three samples contained 16.6% of the speB exotoxin gene. The speG was positive in 4 samples (22.2%) and hasA gene was confirmed in 5 samples (27.8%). The presence of spd3 gene was positive in 4 samples (22.2%). None of the samples carried the Sla gene and only one case (5.5%) was positive for silC gene. Three clinical strains (16.6%) carried 6 or more of the studied factors (TS-48, TS-101 and BC-46). None of the studied genes were found in 12 (66.7%) samples.

Conclusion: This study showed that the prevalence of virulence genes was lower in the collected strains than the global studies. This issue highlights the need for molecular epidemiological studies in Iran with native strains. It is suggested that additional research be conducted with a larger sample size and sampling from a variety of invasive and non-invasive diseases.

Keywords: Streptococcus pyogenes, Pharyngitis, septicemia, virulence factors, PCR

The resistance of breast tumors to tamoxifen , evaluation of therapeutic challenges and a prospective perspective (Review)

Zahra farhoud Khomeirani,[1,*] Sepehr bozorgchenani,[2]

1. department of Veterinary, Rasht branch, islamic azad university
2. Department of Bioinformatics, Tehran branch, Science and Culture university

Introduction: Breast cancer is one of the most common cancers diagnosed among women and is the second leading cause of cancer death among women after lung cancer. breast cancer is a hormone-dependent tumor in which estrogen plays a major role. the goal is to target ER using ER antagonists or antiestrogens. It is a reliable treatment for all stages of the disease in premenopausal and postmenopausal women. in this study we highlighted the role of ER in breast cancer .we discuss breast cancer, especially luminal breast cancer, and the challenges prognosis and resistance of these tumors to selective estrogen receptor modulators such as tamoxifen.

Methods: In this review, we briefly describe the information obtained from the Google Scholar Science Direct database.

Results: On the other hand, The intratumor variability in antiestrogen responsiveness also changes over time, and thus several and complex mechanisms are involved in developing antiestrogen resistance. As mentioned earlier, it should be noted that there is not a single mechanism alone responsible for the development of antiestrogen resistance and it is very likely that resistance comes from various cellular events. Considering the clinical values of tamoxifen in the treatment of breast cancer, it is clear that preventing and overcoming tamoxifen resistance remains an important clinical goal. A better understanding of resistance mechanisms would aid in the development of novel strategies to overcome tamoxifen resistance and provide the basis for breast cancer treatment options.

Conclusion: According to the findings, resistance to hormonal therapies in breast cancer due to the toxicity and carcinogenicity of high doses of tamoxifen and the management of this process by nanomaterials, there are still fundamental challenges regarding the mechanism of action of different cells and biological reactions in nanomaterials exist and require careful evaluation there are several risks to the benefits of nanomaterials.

Keywords: breast cancer, Tamoxifen, estrogen receptor, luminal breast cancer

The role of circular RNAs in stem cell differentiation (Review)

Roqaye Karimi,[1,*] Amir Atashi,[2] Monireh Ajami,[3] Mansoureh Ajami,[4]

1. Department of Hematology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran
2. Stem cell and Tissue Engineering Research Center, Shahroud University of Medical Sciences, Shahroud, Iran
3. Department of Medical Laboratory Sciences, School of Paramedical Sciences, Islamic Azad University Tehran Medical Sciences, Tehran, Iran
4. Department of hematology, School of Allied Medical Sciences, Shahroud University of Medical Sciences, Shahroud, Iran

Introduction: Stem cells are the primary cells that have the ability to differentiate into various types of cells, and it has been proven that stem cells can treat a number of different diseases. Some of the most important applications of stem cells include the repair of damaged heart tissue, bone tissue repair, treatment of nerve and spinal cord injuries, treatment of diabetes, etc. New strategies are needed for stem cell differentiation, one of which is the use of circular RNAs (circRNAs). circRNAs are a group of non-coding RNAs (ncRNAs) that are produced from protein encoding genes through a process called back splicing and are resistant to mRNA-degrading enzymes due to their their circular structure and lack of a 5' cap and a poly-A tail. This resistance has caused circRNAs to have relatively longer stability and half-lives than their linear counterparts and other ncRNAs, including miRNA and LncRNAs, making them potential tools for therapeutic innovative strategies. In general, circRNAs are expressed in eukaryotes and have tissue-/cell-specific patterns. Many studies have suggested that circRNAs play an essential role in important cellular processes, such as evolution and differentiation through post-translational regulation, and their expression disorder is involved in the pathogenesis of a variety of diseases. Along with the development of bioinformatics technology, several circRNAs with important biological functions have been discovered. They act as sponges for miRNAs and subsequently play a major role in regulating stem cell differentiation by regulating the function of miRNAs through their spongy activity. As stem cells are differentiated into mature cells such as neuronal differentiation, myocardial differentiation and osteogenic differentiation, the expression of some circRNAs increases significantly, indicating the importance of circRNAs as biomarkers of stem cell differentiation and a new pathway for stem cell-based therapy.

Methods: We reviewed and analyzed a large number of scientific papers related to the role of circRNAs in stem cell differentiation and the relationship between circRNA and miRNA expression in the differentiation of these cells. Microarray analysis technique was used to identify the expression profile of

circRNAs during the stem cell differentiation. qRT-PCR was used to detect circRNA expression. The function of circRNAs was evaluated by gain- and loss-of-function experiments. Using bioinformatics analysis tools, circRNA-miRNA binding sites, and the target genes of miRNA, were identified.

Results: Several regulatory axes including circ_33287/miR-214-3p/Runx3, circ_0074834/miR-942-5p/VEGF and ZEB1, circ_124534/miR-496/β-catenin, circ_ARHGAP35-circ_2929/miR-204-5p/Runx2 and circ_ITCH-circ_BANP/miR-34a/DUSP1, RAC1 and FAS were identified as essential players in osteogenic stem cell differentiation and bone regeneration. On the other hand, circCACNA1D, circSLC8A1, and circALPK2 played a crucial role in the process of cardiac differentiation of stem cells, and circRIMS2, circRTN4, and CDR1as were involved in the process of neural differentiation of stem cells as well.

Conclusion: To sum up, circRNAs and stem cells have emerged as a novel filed of research. There is ample evidence that the expression of large numbers of circRNAs will change during stem cell differentiation, and several circRNAs play a key role in regulating the differentiation of different stem cell types. Regarding the interaction of circRNAs with miRNAs and their impact on target genes, the identification of circRNA-miRNA-mRNA network has been considered by many researchers today. The impact of miRNAs on the target genes' expression level can be targeted by the spongy effect of specific circRNAs. Exosomes or nanoparticles are recently used as the systems for delivering these molecules into cells. Furthermore, the CRISPR/Cas13 technology and the cre/lox system are used for knocking down circRNAs in stem cells to differentiate them and to develop therapies based on circRNAs. Overall, the circRNAs-miRNAs network plays a major role in regulating stem cell differentiation, which might be a potential new target for the treatment of diseases and suggest the possibility of targeted circRNA therapies in tissue engineering.

Keywords: Circular RNA, circRNA, non-coding RNA, miRNA sponge, stem cell differentiation

The role of CRISPR genome editing technology in the treatment of pancreatic cancer (Review)

Farshid Fathabadi,[1,*]

1. Laboratory Science Research Center, School of Paramedecine, Golestan University of Medical Science

Introduction: Pancreatic cancer is the twelfth most common cancer worldwide and the seventh leading cause of cancer death, with more than 95% of cases associated with pancreatic ductal adenocarcinoma (PDAC). Generally, only less than 10% of patients with pancreatic cancer have an overall survival of more than five years; Consequently, the diagnosis and treatment of pancreatic cancer have become one of the main challenges for researchers. The main treatment options available to patients include; Surgery, chemotherapy, and radiotherapy that; even after treatment by these methods, the disease tends to return after two years, but today newer methods are offered to treat this disease; CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) genome editing technology is one of these methods. As a new approach, CRISPR can use “Cas” proteins that have endonuclease activity to cut the DNA according to the instructions given to them by the sgRNA and modify the gene. CRISPR has become a high-potential tool for gene therapy for many diseases; This technology has lower cost, higher efficiency, and less complexity than other gene therapy methods. Due to the critical role of genetics in tumor formation and development, the use of this tool is essential.

Methods: This article is a review, and we identified its documents by searching for the keywords “pancreatic cancer”, “CRISPR/Cas9” and “CRISPR Technology” in international databases such as “PubMed”, “Google Scholar”, “Scopus”, and “ScienceDirect”. The search period was limited to 2016 to 2021. We found about 55 articles in the initial search, which after further examination, we left out 22 articles with less relevance to the subject. We thoroughly studied 18 articles relevant to the subject from the remaining cases and extracted their results.

Results: The most common mutations in pancreatic cancer are related to KRAS, TP53, SMAD4, CDKN2A genes, which KRAS mutant gene is one of the influential factors in the development of pancreatic cancer; More than 90% of patients with PDAC have this gene mutation, of which the single-site mutation (KrasG12D) is the most common. Both CRISPR/Cas13a and CRISPR/Cas9 systems can play a potentially influential role in preventing the spread of disease by directing sgRNAs and destroying the KRAS G12D mutant gene. Knockdown of HIF-1a, which causes cancer cells to survive under hypoxia, by the CRISPR/Cas9 system effectively inhibits tumor

metastasis and increases patient survival. In a study, the ABCG2 gene was identified as the most stable drug resistance gene in patients chemotherapy; The knockout of this gene by CRISPR can help increase sensitivity and reduce resistance to chemotherapy drugs for pancreatic cancer, including Oxaliplatin. The PSMA6 gene in the PDAC acts as an oncogene, and the CRISPR system can induce apoptosis of pancreatic cancer cells by inhibiting the expression of this gene. Also, in some studies, targeting and deleting the PRMT5 gene by CRISPR technology, combined with Gemcitabine, one of the first-line drugs in pancreatic cancer chemotherapy, had a synergistic effect and inhibited tumor growth, and induced cancer cells death that was detected in both in-vivo and in-vitro studies.

Conclusion: According to the role of various genetic and epigenetic changes in the pathogenesis of pancreatic cancer, CRISPR genome editing technology can be used as a practical and high-potential treatment approach to cure this disease and increase patient survival. However, due to the novelty of this technology, there is a need for more detailed studies and finding more effective options for genetic manipulation in this disease.

Keywords: Pancreatic cancer, CRISPR/Cas9, CRISPR Technology

The role of extracellular vesicles carrying autophagy related miRNAs in AML; In silico analysis (Research Paper)

Majid Gholizadeh,[1] Mahsa TahmasebiVand,[2] Leila Noorazar,[3] Elham Roshandel,[4] Abbas Hajifathali,[5,*]

1. 1Department of Hematology and Blood Banking, School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran / 2Hematopoietic Stem Cell Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
2. Department of Medical Genetics, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
3. 1Department of Hematology and Blood Banking, School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran / 2Hematopoietic Stem Cell Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
4. Hematopoietic Stem Cell Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
5. Hematopoietic Stem Cell Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Introduction: Autophagy is an intracellular degradation system that delivers cytoplasmic constituents to the lysosome to ensures dynamic recycling, homeostasis, and cell survival under stress. However, autophagy plays a wide variety of physiological and pathophysiological roles but its role in tumorigenesis and cancer progression is still developing. It is recently identified that autophagy is associated with hematological disorders such as leukemia. Acute myeloid leukemia (AML) is a fatal hematological neoplasm of myeloid linage with about 27.4 % 5-years survival rate and accounts for 40% of leukemia-related deaths. Drug resistance and relapse are the main causes of treatment failure. Based on recent studies, increased autophagy in malignant cells leads to meet their metabolic needs, and protect them against chemotherapy and enhance the cell's survival. Based on articles several genes are involved in the autophagy process such as ATG5, ATG4D, ATG3, ulk1, LC3, ATG7, Pu1. miRNAs as short non-coding RNAs regulate gene expression at the post-transcriptional level by binding to their target (mRNA) and can modify various biological pathways in cells. miRNAs can be transferred between cells and change the functions of recipient cells. Extracellular Vesicles (EVs) as a cell-to-cell communication tool can carry various biomolecules such as acid nucleic (DNA, mRNA miRNA), hence play a potent role in sharing miRNAs between cells. In this study, we aim to characterize miRNAs that target autophagy-involved genes and their transmission by the AML-derived EVs may have prognostic value.

Methods: For the purpose of this study, the main autophagy genes were collected based on related articles. Then we filtered out micro-RNAs that target each gene from miRWalk®, and miRTarBase® databases. At next we use GALAXY® database to separate the miRNAs that have the most interaction with mentioned genes. Lastly, Vesiclepedia®, ExoCarta®, and EVmiRNA® were used to assess miRNAs that carried inside the extracellular vesicles as cargo.

Results: According to in-silico analysis, 10 miRNAs that target at least 7 autophagy-related genes were selected. Based on the next evaluations in EV databases, we found 5 of 10 miRNAs including hsa-miR-3127-5p, hsa-miR-378c, hsa-miR-423-5p, hsa-miR-493-3p, and hsa-miR-6785-5p which carry by leukemia-derived extracellular vesicles. These miRNAs can transmit to recipient cells as a cargo of EVs and regulate the expression of the autophagy genes.

Conclusion: In this study, we identified the miRNAs that were carried inside the EVs and play a role in the regulation of autophagy genes, ATG5, ATG4D, ATG3, ulk1, LC3, ATG7, Pu1, and BECN1. Autophagy may provide a survival strategy for tumor cells and is considered to be a protective response of cancer cells to stress and chemotherapy agents. Based on our findings leukemia-derived EVs as a potent communication tool can induce drug resistance and increase survival in malignant cells by transmitting autophagy regulatory miRNAs.

Keywords: Extracellular Vesicles, Acute myeloid leukemia, Autophagy, miRNA

The Role of Information and Communication Technology (ICT) in Facilitating Elderly Lives in the Covid-19 Pandemic Crisis: A Narrative Review (Review)

Seyed Mohsen Laal Mousavi,[1,*] Homa HajiZadegan,[2] Fateme Kamjoo,[3] Fariba Moalem Borazjani,[4] Maryam Karami Mozafari,[5] Maryam Alidadi,[6]

1. Department of Health Information Technology, Faculty of Paramedical, Mashhad University of Medical Sciences, Mashhad, Iran
2. Department of Health Information Technology, Faculty of Paramedical, Mashhad University of Medical Sciences, Mashhad, Iran
3. Department of Health Information Technology, Faculty of Paramedical, Mashhad University of Medical Sciences, Mashhad, Iran
4. Department of Health Information Management, School of Paramedicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
5. Department of Health Information Technology, School of Managment and Information Science, Shiraz University of Medical Sciences Shiraz,Fars ,Iran.
6. Department of Health Information Technology, Faculty of Paramedical, Mashhad University of Medical Sciences, Mashhad, Iran

Introduction: Covid-19 spread all over the world, resulting in a social health crisis. The proportion of older people across the globe is growing rapidly and they have potential physical and psychological needs that should be met. As a result of Covid-19 and social distances, older people are at greater risk of loneliness and isolation

Methods: This study is a narrative review performed in 2021. We reviewed and collected papers without a time limit and organized them by topic. The search was performed on electronic databases like google scholar, SID, science direct, PubMed and using the MeSH, keywords including social isolation, elderly, Covid-19, and ICT to find documents about the main purpose of the study

Results: Looking at the research results, the basic needs of the elderly were such as cognitive function or chronic disease management, safety needs such as fall prevention, and social needs such as social participation to reduce loneliness. ICTs can help family members to monitor their old parents, promote social participation, physical activity, and diet. Also, connect elderly people to the outside world, get social support, and help them to access entertainment and hobbies. The roles of technology should respond to the diverse needs of the elderly such as social, safety, and health needs

Conclusion: The development of ICTs to provide services to the elderly is in constant evolution. During the Covid-19 pandemic, lockdown and social

distancing have made the need for emotional and social support among seniors increasingly important. ICT tools can increase social participation, cognition, physical activity, diet, and sleep. Furthermore, compared with real animals or routine care, robots and ICTs improve loneliness, life satisfaction, social support, quality of life, and other responses. It is emotionally effective and can play an important role in preventing social isolation for the elderly during the Covid-19 pandemic. Cost-effectiveness and availability are two important features that should be considered in the design and application of ICTs.Practical ICT solutions for the elderly in general are used in diseases so disease management and improving the quality of the elderly's life should be considered

Keywords: COVID-19 - Elderly - ICT (Information and Communication Technology) - Social Isolation

The role of NEAT1 in paraspeckle formation and DNA damage repair system (Review)

Kimia Asghari,[1] Soheila Rahgozar ,[2,*]

1. University of Isfahan
2. University of Isfahan

Introduction: A long nontranslating RNA is any RNA that is longer than 200 nucleotides (nt). In mammals, several long non-coding RNAs (lncRNAs) are transcribed from the genome, however, these lncRNAs do not code for proteins. The mRNA stability, translation, and post-translational modifications in the cytoplasm contribute to their regulatory effects on gene expression networks through controlling the nuclear architecture and DNA transcription. NEAT-1 (Nuclear paraspeckle assembly transcript 1) is a functionally conserved long non-coding RNA that has been reported to be frequently deregulated in several types of cancer. This gene is located within the human chromosomal region 11q13 and may function as a regulatory factor for various genes and pathways. It also functions as a core component of the paraspeckle in the nucleus. NEAT1 encodes two transcripts, NEAT1_1 and NEAT1_2, which differ in how their 3'untranslated regions (UTRs) are processed. NEAT1_1 is generated by polyadenylation and produces a 3.7 kb transcript. NEAT1_2 forms a triple helix structure that is then cleaved by RNase P into a 23 kb transcript. Different functions are performed by each of these isoforms. Unlike NEAT1_1, NEAT1_2 is not only required for the formation of paraspeckles but is a limiting factor which controls the tendency of the nucleus for creating certain number of paraspeckles according to its concentration. Paraspeckles are dynamic and membraneless nuclear bodies that can influence cellular functions, including stress response. Paraspeckles have been demonstrated to have at least three main functions at the molecular level. Firstly, they are responsible for the biogenesis of microRNAs, a function which is related to NEAT1 and SFPQ (splicing factor proline- and glutamine-rich) protein. Their second role is gene regulation through the adenine to inosine editing process mediated by the adenosine deaminase enzyme RNA specific. Thirdly, paraspeckles act as molecular sponges which trap RNA-binding proteins, therefore modulating gene expression. Paraspeckles are RNase-sensitive structures, therefore, their transcription is dependent on RNA Polymerase II, suggesting that RNAs are necessary for their maintenance. NEAT1_2 is an essential and architectural lncRNA that acts as a scaffold for paraspeckle assembly. Speckles formation initiates by directly binding some paraspeckle proteins (PSPs) also known as RNA binding proteins, to the NEAT1_2 variant, assisting its stabilization and avoiding its possible degradation. Subsequently, Other PSPs form and eventually SWItch/Sucrose Non-Fermentable (SWI/SNF) chromatin-remodeling complex mediates the protein-protein interaction network required

for paraspeckle assembly, by linking 50 ribonucleoprotein complexes together with NEAT1_2. Various endogenous and exogenous stresses constantly damage DNA, including UV light, ionizing radiation, and reactive oxygen species (ROS). NEAT1 is known as the lncRNA which may regulate the DNA damage repair (DDR) system through multiple signaling pathways, including the ATM and ATR pathways, and the p53 pathway. P53 can be activated by a variety of stress signals, such as DNA-damaging agents, high levels of ROS and hypoxia. In the presence of functional p53, NEAT1_2 is induced followed by DNA damage. It is reported that silencing NEAT1_2 may accumulate DNA damages. It is noteworthy to know that almost all essential PSPs are actively involved in various DDR pathways, such as DNA double-strand breaks. NEAT1 knockdown cells showed decreased ATR-mediated phosphorylation of checkpoint kinase Chk1 and replication protein RPA32, demonstrating that NEAT1 is critical for ATR signaling and checkpoint activation.

Methods: The role of NEAT1 has been investigated by RNA extraction and real-time quantitative PCR, protein extraction and Western blotting, cell cultures and transfection.

Results: lncRNA can regulate the DDR system through the ATM, ATR and the p53 pathway. Many signals can activate p53, which in its turn, may induce the expression of NEAT1_2 and lead to the assembly of PSPs and the formation of paraspeckles.

Conclusion: The current study indicates that cellular stress conditions, known as potential activators of DDR pathways, may stimulate NEAT1 transcription, meanwhile, and initiate the formation and expansion of paraspeckles.

Keywords: lncRNA; NEAT1; paraspeckle; DNA damage repair;

The role of P4HB and related ncRNAs in bladder cancer: an in silico analysis. (Research Paper)

Fahime Nazarpour,[1,*] Mahdieh Khojasteh,[2] Amirhossein Hajialiasgary Najafabadi,[3] Reza Karimnia,[4] Mohammadhossein Naderkhani,[5]

1. Isfahan university
2. Isfahan university
3. Isfahan university
4. Isfahan university
5. Isfahan university

Introduction: Background: Bladder cancer (BLCA) is a malignancy that is known to be fatal, with a 5-year survival rate of 77 percent. For the time being, the function of single nucleotide polymorphisms (SNPs) in associated noncoding RNAs (ncRNAs) with the genes implicated in BLCA is a new area of concern. The associations between one of the prognostic markers in BLCA and ncRNAs, as well as related SNPs, were investigated in the current study.

Methods: Method: First of all to display pertinence between BLCA and ncRNAs, a reliable prognostic marker was detect by searching from other articles. To investigate the highly differentially expressed genes and prognostic marker for BLCA, GEPIA2 was applied. LncRNASNP2 database was used to detect variants of these molecules related to the mentioned gene. miRNA assessment was proceeded by investigation of miRNAs by using miRWalk. Pathway analysis was performed based on other target genes of two mentioned miRNAs to assess whether they contribute to BLCA or not.

Results: Result: By investigation in different studies, P4HB was recognized as a prognostic marker that was upregulated in BLCA patients against normal. There is no validated evidence for lncRNA interaction with our candidate gene. Two miRNAs, hs-mir-4292 and hs-mir-4308 were detected that aimed P4HB as a target. pathway analysis of other target genes of chosen miRNAs, revealed that both of them participate in BLCA related pathways and malignancy of cancer.

Conclusion: Conclusion: Our finding indicated P4HB and its associated ncRNAs are able to participate in a prognosis diagnosis, and invasiveness of BLCA.

Keywords: in silico, BLCA, ncRNAs, miRNAs, prognostic marker

The Role of Parenteral Nutrition in Hodgkin's Lymphoma (Review)

Mojtaba Hajipour,[1] Zahra Hamidi,[2] Erfan Imani,[3] Ali Mortezaei,[4] Hojjat Shadman Zahroodi,[5,*]

1. Bachelor student of Nutrition, Department of Nutrition Sciences, Varastegan Institute for Medical Sciences, Mashhad, Iran.
2. Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran
3. Student Research Committee,Esfarayen Faculity Of Medical Science, Esfarayen, Iran
4. Student Research Committee, Gonabad University of Medical Science, Gonabad, Iran.
5. 1.. student research committee, Mashhad University of Medical Sciences, Mashhad , Iran 2.master student of medical education, Virtual School of Medical Education and Management, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Introduction: Hodgkin disease, often known as Hodgkin lymphoma, is a malignancy which can develop through lymph system and spread to various regions of the body(1). Both children and adults can develop the disease, but it's most common in early adulthood and the risk of developing this disease rises again in late adulthood(2). Signs and symptoms of this disease may include painless swelling of lymph nodes around neck, armpits or groin, persistent fatigue, fever, night sweats, severe itching and unexplained weight loss(3). Nevertheless, there is a valid point to be made regarding this condition, the medication is quite efficient, and the majority of cases are curable(4). Malnutrition is usually observed in cancer patients and unfavorably affects the quality of life and survival of them(5).To avoid the disorders associated with malnutrition, nutritional support required for these patients(6). As a consequence, enteral nutrition or parenteral nutrition should be provided to these individuals(7). Parenteral nutrition is a method of getting nutrition inside the body through the veins. Depending on which vein is used, this procedure is referred to as either total parenteral nutrition (TPN) or peripheral parenteral nutrition (PPN). This form of nutrition is often used for people with crohn's disease, cancer, short bowel syndrome and ischemic bowel disease(8). Benda-EAM or BEAM is a second-generation regimen that has been widely used since 1990 for autologous stem cell transplantation in patients with recurrent or refractory lymphoma. It contains carmustine [BCNU], etoposide, cytarabine, and melphalan.(9) The high prevalence of malnutrition in patients with cancer, as well as the necessity of nutrition assistance in these patients, encourages us to investigate parenteral nutrition can cover the nutritional requirement of patients with Hodgkin lymphoma disease.

Methods: To accomplish this narrative review, we searched four Databases (PubMed, Web of Science, Scopus and google scholar) based on the search strategy from 2010 to 2021 with the high sensitivity on September 2021 by following MeSH keywords: Hodgkin's Lymphoma, Hodgkin's Lymphoma, Hodgkin Lymphoma, Hodgkin Disease, Parenteral nutrition, Parenteral Feeding, Intravenous Feeding

Results: Publications on parenteral nutrition and Hodgkin's disease, which examined a total of 539 patients, found a clear link between treatment for Hodgkin's disease and injectable nutrition and symptom alleviation. Parenteral nutrition with the BEAM regimen (carmustine [BCNU], etoposide, cytarabine, and melphalan) in patients with recurrent or refractory lymphoma for autologous stem cell transplantation can be associated with positive results for neutrophil and platelet transplantation. However, caution is necessary because an increase in the frequency of grade 3 mucositis was observed in the Benda-EAM group (82.4 v vs. 48).Also, the Benda-EAM regimen in these patients, with a total dose of 320 mg / m2 (160 mg / m2 in two days) can be helpful and treatment with this Dosage may reduce the risk of bandamostine-associated renal and cardiac toxicity. (9) Parenteral nutrition can substantially decrease the incidence, severity, and course of oral mucositis, which is a common but serious complication of hematopoietic stem cell transplantation, as well as neutropenic enterocolitis (a rare but serious complication of chemotherapy).(10)(11) In patients undergoing hematopoietic stem cell transplantation for resistant or refractory primary lymphoma, intravenous feeding reduced the mean days of myeloid transplantation (10 vs 11; P = 0.014) and platelet transplantation (13 vs 15; P = 0.006). And reduce the risk of neutropenic sepsis and short-term hospitalization.(12)

Conclusion: Our results show that there is an effective association between parenteral nutrition and Hodgkin's disease so that it can reduce the length of hospital stay and the symptoms of the disease as a result of chemotherapy, but up to date not enough studies have been done on this subject. Most journals are case studies, so more research is needed in the future to get more accurate results.

Keywords: Hodgkin's Lymphoma, Parenteral nutrition, Intravenous Feeding

The role of parenteral nutrition in non-Hodgkin's lymphoma (Review)

Ali Mortezaei,[1] Zahra Hamidi,[2] Erfan Imani,[3] Mojtaba Hajipour,[4] Hojjat Shadman Zahroodi,[5,*]

1. Student Research Committee, Gonabad University of Medical Science, Gonabad, Iran
2. Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran
3. Student Research Committee,Esfarayen Faculity Of Medical Science, Esfarayen, Iran
4. Bachelor student of Nutrition, Department of Nutrition Sciences, Varastegan Institute for Medical Sciences, Mashhad, Iran
5. 1.. student research committee, Mashhad University of Medical Sciences, Mashhad , Iran 2.master student of medical education, Virtual School of Medical Education and Management, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Introduction: Non-Hodgkin's lymphoma is a type of cancer that begins in the lymphatic system. In this disease, white blood cells called lymphocytes grow abnormally and form tumors throughout the body(1). Non-Hodgkin's lymphoma includes many subtypes. follicular lymphoma and Diffuse Large B-cell lymphoma are among the most common subtypes. Almost 90% of Non-Hodgkin's lymphoma cases are of B-cell origin(2). Signs and symptoms of this disease is almost the same as Hodgkin disease: painless swelling of lymph nodes around neck, armpits or groin, fever, persistent fatigue, night sweats, severe itching and unexplained weight loss(3). Medications that suppress the immune system increase the risk of developing non-Hodgkin's lymphoma. There are other risk factors such as chemicals, infection with certain viruses and bacteria and age (the risk increases with age)(1). Malnutrition is the common complication of cancer. Even, cancer cachexia may be the result of Cancer-related malnutrition(4).So nutrition support should be given to these patients through enteral nutrition or parenteral nutrition(5). Parenteral nutrition is a method of getting nutrition inside the body through the veins. Depending on which vein is used, this procedure is referred to as either total parenteral nutrition (TPN) or peripheral parenteral nutrition (PPN). This form of nutrition is used to help people who can't or shouldn't get their core nutrients from food such as cancer patients(6). The high prevalence of malnutrition in cancer patients and the importance of nutrition support in them, encourage us to check if the parenteral nutrition can meet the nutrition needs of patients with non-Hodgkin's lymphoma.

Methods: To accomplish this narrative review, we searched four Databases (PubMed, Web of Science, Scopus and google scholar) based on the search strategy from 2010 to 2021 with the high sensitivity on September 2021 by

following MeSH keywords: Non-Hodgkin's Lymphoma, Non-Hodgkin's Lymphoma, Non-Hodgkin's Lymphoma, B-Cell Lymphoma, Follicular Lymphoma, Small Noncleaved Cell Lymphoma, Parenteral nutrition, Parenteral Feeding, Intravenous Feeding

Results: Result from 3 randomized and controlled trials, 1 case series and 3 case studies which include 553 patients were evaluated. Publications on parenteral nutrition and Hodgkin's disease have established a direct relationship between non-Hodgkin's disease therapy and symptom alleviation. total parenteral nutrition may assist to minimize the adverse effects of some medications used to treat Follicular B Cell Lymphoma (such as Rituximab) and accelerate the time it takes for the medication to operate(7). Nevertheless, in relapsed and refractory lymphoma transplants, those treated with lomustine, cytarabine, cyclophosphamide, and etoposide (LACE) had a significantly lower parenteral nutrition requirement (32 vs 69 %; P 0.001) than any of those treated by BCNU, etoposide, cytarabine, and melphalan (BEAM).(8) Total parenteral nutrition is strongly recommended and necessary for the treatment of oral mucositis(9), one of the significant adverse effects of hematopoietic stem cell transplantation, as well as Neutropenic enterocolitis(10), one of the consequences of intensive chemotherapy. Our finding indicated that using total parenteral nutrition in individual with non-Hodgkin's lymphoma can increase oral intake, energy (27% to 70%) and protein requirements (23% to 77%)(11); nevertheless, despite the increased energy and protein supplementation provided by parenteral nutrition, the patients' nutritional status did not improve before the chemotherapy, on the other hand, the nutritional situation, was not worsening(7)(11). The integration of total parenteral nutrition and other nutritional interventions may enhance the efficacy of treatment and improve the prognosis of non-Hodgkin's lymphoma and maybe effective on the treatment of non-Hodgkin's lymphoma's clinical symptoms, complications of intensive chemotherapy and transplantation(7)(11)(12)(13).

Conclusion: In conclusion, in order to prevent additional worsening of nutritional condition as a consequence of chemotherapy and allow the planned chemotherapy in a non-Hodgkin lymphoma patient total parenteral nutrition for each situation may be necessary. There haven't been enough studies done on this issue lately, and the bulk of the publications are case studies, hence future research is needed in the future to get more accurate results.

Keywords: Non-Hodgkin's Lymphoma, Parenteral nutrition, Intravenous Feeding

The role of plastic surgery and self-care during an epidemic covid 19 (Review)

Elnaz Abedini,[1,*]

1. ANKARA UNIVERSITY

Introduction: The Sars-Cov-2 virus is characterized by a being highly contagiousness, and this is the reason why massive use of personal protective equipment is required by medical and paramedical staff of the COVID-19 dedicated departments. The aim of this manuscript is to describe and share our experience in the prevention and treatment of the personal protective equipment related pressure sores and other skin alterations in the medical and paramedical staff..Based on high quality surgery and scientific data, scientists and surgeons are committed to protecting patients as well as healthcare staff and hereby provide this Guidance to address the special issues circumstances related to the exponential spread of the Coronavirus disease 2019 (COVID-19) during this pandemic.

Methods: The aim is to take responsibility and to provide guidance for surgery during the COVID-19 crisis in a simplified way addressing the practice of surgery, healthcare staff and patient safety and care. It is the responsibility of scientists and the surgical team to specify what is needed for the protection of patients and the affiliated healthcare team. During crises, such as the COVID-19 pandemic, the responsibility and duty to provide the necessary resources such as filters, Personal Protective Equipment (PPE) consisting of gloves, fluid resistant (Type IIR) surgical face masks (FRSM), filtering face pieces, class 3 (FFP3 masks), face shields and gowns (plastic ponchos), is typically left up to the hospital administration and government.

Results: Various scientists and clinicians from disparate specialties provided a Pandemic Surgery Guidance for surgical procedures by distinct surgical disciplines such as numerous cancer surgery disciplines, cardiothoracic surgery, ENT, eye, dermatology, emergency, endocrine surgery, general surgery, gynecology, neurosurgery, orthopedics, pediatric surgery, reconstructive and plastic surgery, surgical critical care, transplantation surgery, trauma surgery and urology, performing different surgeries, as well as laparoscopy, thoracoscopy and endoscopy.

Conclusion: Any suggestions and corrections from colleagues will be very welcome as we are all involved and locked in a rapidly evolving process on increasing COVID-19 knowledge.

Keywords: Coronavirus, COVID-19, Dermatology, Elective surgery, Emergency, PPE

The role of stem cells in brain damages and Parkinson's disease (Review)

fatemeh andarbay,[1,*]

1. Dezful Azad University

Introduction: A stem cell is a low-differentiation cell that has the ability to divide and replicate itself indefinitely (often throughout the life of an organism) and, under the right conditions, can differentiate and become a type of cell in a living organism. In the 1960s, scientists studying mice discovered two areas of the mouse brain that had dividing cells, and the resulting cells could turn into nerve cells, and years later found that the adult brain also had stem cells. Which are activated with the onset of disease or tissue damage.Stem cell classification based on differentiation power: 1) All-Power Stem Cells: These cells have the ability to become a variety of cells and tissues that make up the fetus. These cells are the most common type of stem cell. 2) Pluripotent stem cells: These cells have the ability to differentiate into any cell in vitro but do not have the ability to form extracellular cells (placenta). 3) Multiple stem cells: This type of cell has the ability to differentiate into more limited types of cells and can not form a complete embryo and are known as adult stem cells.Neuronal stem cells are mature stem cells that are multipotent and can differentiate into neurons and glial cells and can be obtained from the spinal cord and anterior brain. Stem cell growth in the laboratory can be accomplished through cell culture, and in the differentiation phase, ectodermal cells can be differentiated into neurons using neuronal growth factors. It is only important to note that in uncontrolled conditions these cells may be tumorigenic Parkinson's is a debilitating and progressive neurodegenerative disease Symptoms: slowness of movement, stiffness, muscle tremors, imbalance, difficulty swallowing and speaking The main pathology in this disease is the destruction or disintegration of nerve cells The most common treatment for this disease in humans is the use of l-dopa and carbidopa drugs.At first, the researchers used their cell therapy in relation to this neurological disorder on an animal model, and in all of them, they achieved good results, such as: Stem cells can be used to regenerate brain cells in patients with Parkinson's. Researchers in mice injected embryonic stem cells into the brains of mice with Parkinson's disease and found that the stem cells improved the mice. Clinical studies on the therapeutic effect of human embryonic mesenchymal stem cells have been shown to be effective in improving the patient because these transplanted cells were able to secrete dopamine. On the other hand, studies have shown that 7 to 15% of patients who have been transplanted have a slow movement that can be due to disrupted neurogenesis or the presence of chronic inflammation due to the immune response at the transplant site.

Methods: By study and review articlrs

Results: Cell therapy for the treatment of neurodegenerative disorders is in its early stages and still has room for improvement. There are many fundamental issues that need to be addressed. For example, recognizing the molecular properties of stem cell proliferation to cause genetic changes in ESCs (embryonic stem cells) and better development of NSCs (nerve stem cells) is one of the concerns today.

Conclusion: The study and comparison of different types of stem cells in the treatment of Parkinson's disease to some extent refers to the more effective role of nerve stem cells and umbilical cord stem cells in the treatment of the disease.

Keywords: Stem cells. Nerve tissue. treatment . Parkinson's disease

The role of stem cells in the treatment of heart disease (Review)

fatemeh andarbay,[1,*]

1. Dezful Azad University

Introduction: Different tissues in the body are made up of cells, some of which have the ability to regenerate cells of the same type, including heart cells and the nervous system. These cells have two distinct characteristics; 1) Under the influence of suitable conditions, they can become other specialized cells of the body. 2) They have the ability to make their own stem cells and they divide during many divisions and in a long time without change. In conditions such as events after a heart attack, chronic heart failure or heart muscle destruction, the heart will no longer have adequate contractile power. Medication, heart transplant, etc. are common treatments. The last recommended treatment is myocardial cell repair, in which stem cells are transferred into the myocardium, and by providing the right conditions, attempts are made to produce new heart cells and regenerate the damaged area. . Bone marrow cells, embryonic cells, deceased donor muscle cells, smooth or striated muscle cells, embryonic heart cells, umbilical cord blood, and peripheral blood have been used for cell transplantation in the heart muscle. Using induction, it differentiates embryonic mesoderm cells and can be used to differentiate bone, muscle, blood, cartilage and graft cells. Cardiomyocytes can be obtained by using pure culture media such as matriogel or cardiogel or by co-culture or co-culture with some compounds or tissues. Research suggests that the best cellular sources for treating damaged heart muscle are skeletal muscle cells and bone marrow cells that need to be cultured. These cells are also resistant to fatigue and ischemia. Myoblasts (skeletal muscle cells) are a collection of muscle cells that are easily obtained through biopsy, and are the individual's own adult stem cells that are neither repelled by the immune system nor morally challenged to use. Bone marrow cells also stimulate angiogenesis. These cells can be injected into the blood vessels in the affected area through the catheter, or injected directly into the heart muscle through open surgery or thoracoscopy (both methods are allowed in Europe). There is a risk of embolism with intravascular injection. In the direct method, there is a possibility of heart rupture, especially in heart attacks. Stem cells are also injected with substances that improve telomerase activity, promote stem cell localization, and improve stem cell growth. The most important concern of researchers in such clinical trials is the lack of electrical communication between the implanted cells and other heart cells, which can cause arrhythmias. That's why they put an automatic cardiac defibrillator inside the heart; This method has been approved as a treatment method.

Methods: by study and review artical

Results: Humans have long been aware of the existence of cells and have done a lot of research, but they still do not know much about the function of various cells, especially stem cells. On the other hand, there are countless questions in the minds of researchers, and this may mean that cell therapy is not currently recommended as a comprehensive clinical method, but researchers hope that this method will replace heart transplantation in the near future.

Conclusion: Myoblasts and bone marrow cells can be injected into the heart muscle to improve heart function (both methods are allowed in Europe).

Keywords: treatment . Heart tissue. Stem Cells

The SP/NKR1 induction as the suppressible metastasis inducer by aprepitant antagonistic impact on human colorectal SW480 cancer cells (Research Paper)

Malihe Golestaneh,[1,*] Mohsen Firoozrai,[2] Seyed Isaac Hashemy,[3] Hossein Javid,[4]

1. Student Research Committee, Clinical biochemistry Department, Medical faculty, Shahrood Azad University
2. Professor, Clinical biochemistry Department, Medical faculty, Shahrood Azad University
3. Surgical Oncology Research Center, Mashhad University of Medical Sciences, Mashhad
4. Department of Clinical Biochemistry, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Introduction: Substance P (SP)/ neurokinin-1receptor (NK1R) as the key metastasis signaling pathway can be targeted by substance P antagonists to prevent its cancer-progressive impacts. In the current study, we aimed to investigate the carcinogenic activity of SP/system in human SW480 colorectal cancer cells and study the antagonistic impact of aprepitant (AP) by measuring MMP-2 and MMP-9 enzymatic activity.

Methods: Different concentrations of SP alone and mixed by AP were exposed to the SW480 cell line to investigate the cells' viability and metastasis by applying Resazurin and Gelatin Zymography methods, respectively. The cells metastatic response was analyzed by measuring the MMP-2 and MMP-9 in both transcription and translation levels. Finally, the Scratch Assay was carried out to evaluate the cells' metastatic response following SP/AP treatment doses.

Results: A significant metastatic activity was observed in SW480 cells following the increasing SP treatment doses by detecting MMP-2/MMP-9 enzyme activity, genes overexpression, and enhanced cell migration. This is while the AP treatment doses meaningfully diminished all the SP-mediated metastatic impacts (p-Value<0.001).

Conclusion: According to the results, the SP/NKR1 signaling pathway has the potential to be considered as one of the main metastatic effectors in human colorectal cancer. Moreover, the AP compound is suggested to be used as the SP antagonist and an efficient anti-metastatic compound.

Keywords: metastasis signaling pathway; SP antagonist; Aprepitant; anti-metastatic compound; colorectal cancer

The study of NGF, PAX3 and NSE genes expression in bone marrow-derived mesenchymal stem cells after treatment by glabridin for differentiation into nerve-like cells (Research Paper)

Fatemeh Tahmasebimoghadam,[1] Hossein Fahimi,[2,*] Hora Jalali Tehrani,[3]

1. Department of Developmental Biology, Faculty of Advanced Science and Technology, Tehran Medical sciences , Islamic Azad university ,Tehran, Iran
2. Department of Genetics, Faculty of Advanced Science and Technology, Tehran Medical sciences , Islamic Azad university ,Tehran, Iran
3. Department of Developmental Biology, Faculty of Advanced Science and Technology, Tehran Medical sciences , Islamic Azad university ,Tehran, Iran

Introduction: Glabridin is an essential iso-flavonoid extracted from Licorice root and has antioxidant and neuroprotective functions. As the in-vitro differentiation potential of bone marrow-derived mesenchymal stem cells into the nerve-like cells is approved, glabridin effect on the differentiation of these cells will be analyzed via assessment of effective genes expression level to make a way to repair the nerve system defects.

Methods: Human bone marrow-derived mesenchymal stem cells were induced using 5, 10, 20, 40, and 80 µm glabridin concentrations for 24 hrs. The toxicity of glabridin was assessed using MTT assay and cell morphologies were observed using inverted optical microscopy. Alteration of NGF, PAX3and NSE genes expression were assessed using the Real-time PCR method.

Results: MTT results showed that cell death occurred in 40 and 80 µm doses. Based on the performed analysis, during the 24hrs treatment, NGFand NSE genes expression levels at the case group increased in comparison to the control group, though, the expression level of the PAX3 gene has significant decrease.

Conclusion: The present results showed that the bone marrow-derived mesenchymal stem cells treatment using glabridin resulted in the NGFand NSE genes expression enhancement, and PAX3 gene expression reduction via enhancement of their differentiation into the nerve-like cells. Therefore, glabridin could be used in the differentiation of bone marrow-derived mesenchymal stem cells into nerve-like cells.

Keywords: Mesenchymal stem cells, Bone marrow, Nerve-like cells, Glabridin.

The study of XBP1s factor as an indicate of ER stress pathway in tumor tissue of patient with colorectal cancer in compared to their margins from 1396 to 1398 in Imam Khomeini hospital (Research Paper)

Mohammadkian zarafshani,[1] Marveh rahmati,[2,*] Habibolah Mahmoodzadeh,[3] Vahid Soleimani,[4] Ahad Mohammadnejad,[5]

1. Tehran University of Medical Sciences School of Medicine, Department of General Surgery ,Cancer Institute of Iran , Cancer Biology Research Center.
2. Tehran University of Medical Sciences School of Medicine ,Cancer Institute of Iran , Cancer Biology Research Center.
3. Tehran University of Medical Sciences School of Medicine, Department of General Surgery ,Cancer Institute of Iran
4. Assistant Professor of Pathology Department of Pathology, School of Medicine Cancer Institute Tehran University of Medical Sciences
5. Tehran University of Medical Sciences School of Medicine ,Cancer Institute of Iran , Cancer Biology Research Center.

Introduction: Colorectal cancer (CRC) is one of the most common cancers with increasing mortality in Iran and the world. Despite new treatments relapse, drug resistance, and poor prognosis are some of the major challenges in patients with CRC. Recently, endoplasmic reticulum stress pathway (ER STRESS), especially XBP1s, has been emphasized as an important factor in the pathogenesis and targeted treatment of many types of cancer. Therefore, the aim of this project was to evaluate the expression of XBP1s as an indicator of the stress pathway of the ER stress in tumor tissues of patients with CRC compared to their tumor margins.

Methods: For this purpose, 91 Formalin-Fixed Paraffin-Embedded tissue sections of patients with CRC and 6 blocks of tumor margins as normal tissue were collected from tumor bank of Imam Khomeini Hospital in Tehran. XBP1s expression was measured by tissue microarray. Data analysis was performed using SPSS20 software with Chi-squared, Fisher exact and Kruskal-wallis test. In all experiments, $p \leq 0.05$ was considered statistically significant.

Results: Statistical analysis showed that there is a significant relationship between the expression of XBP1s in tumor tissues with the variable TNM (CLINICAL STAGE) and the degree of differentiation, (P value <0.05).

Conclusion: In conclusion ER stress pathway can be introduced as an indicator of diagnostic and therapeutic potential in colorectal cancer.

Keywords: Colorectal Cancer (CRC), Endoplasmic reticulum stress, tissue microarray, XBP1s

Theoretical and experimental study of the trehalose and myo-inositol mixed osmolytes on thermal stability of recombinant urate oxidase enzyme (Research Paper)

Reihaneh Samareh-Hoseinalinejad,[1,*] Maryam Zaboli,[2] Masoud Torkzadeh-Mahani,[3]

1. Department of Biotechnology, Institute of Science, High Technology and Environmental Sciences, Graduate University of Advanced Technology
2. b Department of chemistry, Faculty of science, University of Birjand
3. a Department of Biotechnology, Institute of Science, High Technology and Environmental Sciences, Graduate University of Advanced Technology

Introduction: Today, due to the wide application of enzymes in various industries, the stabilization of enzymes in order to maintain their activity under different conditions has attracted a lot of attention. Enzyme urate oxidase or uricase (EC: 1.7.3.3) is an enzyme of the oxidoreductases family that catalyzes the oxidation of uric acid to 5-hydroxy isovarate and releases CO2 and H2O2. 5. Hydroxy isovarate is an intermediate compound that is converted to allantoin through several stages of enzymatic or chemical reaction, which is 5 to 10 times more soluble in water than uric acid. Uricase is present in most organisms and microorganisms, but some primates and Reptiles have lost uricase gene activity during the development of their genomes due to mutations. The concentration of uric acid in human serum is 6-1.5 for women and 7-2.5 for men. Any increase in purine catabolism or a decrease in uric acid excretion leads to the formation of monosodium urate (MSU) crystals in the joints or soft tissues, leading to hyperuricemia (a common feature of Tumor Lys Syndrome (TLS) and gout). Gout presents with painful inflammation of the joints, deposition of sodium urate crystals, and uric acid kidney stones. Uric acid is naturally the product of the catabolism of purine nucleotides. Osmolytes are small organic compounds found naturally in living cells that protect the cell from osmotic stress. Osmolytes contain amino acids, methylene amines and polyols. Polyols also contain glycerol, sucrose and trehalose and other sugars such as inositol. Osmolytes stabilize the protein structure and protect their natural form from being disturbed.

Methods: First, the urate oxidase coding sequence was subcloned into PET.28a expression vector and after induction with IPTG inducer, the recombinant protein was purified by affinity chromatoghraphy. In order to prove the protein expression, the samples were loaded on 10% SDS-PAGE gel and single protein bands in the range of 35 kDa was observed and also the concentration of the purified enzyme was determined using Bradford method. To measure the activity of the enzyme, we used its ability to break down uric acid molecules and reduce its absorption at 293 nm. we applied response surface methodology for prediction of the optimal incubation

temperature, the concentration of trehalose and myo-inositol and the incubation time of mixed osmolytes with uricase enzyme. In the following, the activity of treated enzyme measured under recommended condition.

Results: The best enzyme activity in the different treated condition was observed in a mixture of 12.5 mM myo-inositol and 1.125 mM trehalose at 21.25 ° C and 35 minutes incubation time .

Conclusion: To increase stability, many approaches can be take into account, such as mutations or genetic manipulation, chemical modifications, stabilization, and the use of additives, one of which is osmolytes. The results showed that the addition of 12.5 mM myo-inositol and 1.125 mM trehalose had the maximum effect on uricase enzyme stability

Keywords: uricase, osmolytes, terhalose, myo-inositole

Therapeutic effects of herbal medicine on beta-coronavirus infections (Review)

Mohaddeseh Larypoor ,[1,*] Tina Zarrinpanah ,[2] Fatemeh Fardi,[3] Sina Yaghoubi,[4]

1. Assistant Professor of Mycology , Department of Microbiology, Faculty of biological science, Islamic Azad university, Tehran north branch, Tehran, Iran
2. PhD students, Islamic Azad University, Kish branch, Iran
3. PhD students, Islamic Azad University, Kish branch, Iran
4. PhD students, Islamic Azad University, Kish branch, Iran

Introduction: Background & Objectives: Medicinal plants have been considered by many researchers because of their various compounds, including secondary metabolites, which can act as an alternative to chemical drugs. Infectious diseases of viral origin such as influenza, herpes, hepatitis C and Beta corona virus are among the viral diseases. In this article, we review the use of herbs to treat influenza, herpes, hepatitis C and Beta corona virus. The work done by various researchers on effective plants has been reviewed. Also, various forms of medicine such as essential oil of aqueous extract, alcoholic extract, etc. in the treatment of these types of viruses have been reviewed and discussed.

Methods: In this article, we review the use of herbs to treat influenza, herpes, hepatitis C and Beta corona virus. The work done by various researchers on effective plants has been reviewed. Also, various forms of medicine such as essential oil of aqueous extract, alcoholic extract, etc. in the treatment of these types of viruses have been reviewed and discussed.

Results: Findings indicate that the use of medicinal plants derived in different forms (alcoholic extract, aqueous extract, etc.) can be useful in the treatment of influenza, herpes, hepatitis C and Beta corona virus. Also, studies have shown that the side effects of using these drugs are very low.

Conclusion: Medicinal plants can be used to treat viruses as potential treatments with less side effects to be considered.

Keywords: Covid-19, hepatitis C, proteinase, genome

Therapeutic Potential of Stem Cells in Emerging and Epidemic-Prone Diseases Inspired by Experiences from COVID-19 Pandemic: A Review (Review)

Omid Miri,[1,*] Alireza Alavi Moqadam,[2] Amirhossein Kaffash,[3]

1. Shahid Beheshti University
2. Shahid Beheshti University
3. Shahid Beheshti University

Introduction: The declarations of the emergency situation by the Up to now, World Health Organization (WHO) has declared emergency situation due to several extensive outbreaks of infectious diseases, especially in the new century. Considering this fact, as well as the mortality of these outbreaks and the chance of future re-emergence, have prompted researchers to seek effective therapeutic strategies for proper management of infectious, epidemic-prone diseases. One of these strategies is the application of stem cells, showing good effectiveness in the Coronavirus Disease 2019 (COVID-19) pandemic. The present review aimed to investigate the latest available literature on the therapeutic potential of stem cells in outbreaks caused by the following viral diseases: Severe Acute Respiratory Syndrome (SARS, 2003), Influenza (2009), Middle East Respiratory Syndrome (MERS, 2012), Ebola Virus Disease (EVD, 2014), Zika Virus Disease (ZIKV, 2016), and COVID-19 (2019).

Methods: In order to find the studies on the therapeutic potential of stem cells on the mentioned epidemic-prone diseases, the databases of Google Scholar, PubMed, and Scopus were searched using the following keywords and phrases: "stem cells and SARS-CoV", "stem cells and SARS-CoV-2", "stem cells and MERS-CoV", "stem cells and Ebola virus", "stem cells and Influenza virus", and "stem cells and Zika virus". A total of 125 studies, which were published before July 11, 2021, were collected. Afterward, the related abstracts and titles were evaluated, and the duplicated studies were omitted. Moreover, those not following our eligibility criteria were omitted. Eventually, 78 studies were selected for translation and complete analysis. The data on the effectiveness and side effects of this therapeutic intervention were classified in a table and underwent analysis.

Results: According to our findings, stem cells and their derivatives, such as exosomes, can be used as an effective therapeutic strategy for COVID-19. There are several ongoing and completed clinical trials on this topic. Various types of stem cells, especially mesenchymal stem cells, are used to manage the fatal complications of these diseases, such as ARDS (Acute Respiratory Distress Syndrome). However, there is limited research on the efficacy of stem cells in SARS and MERS, which are highly similar to COVID-19 in

pathogenesis. Moreover, the literature on stem cell therapy in influenza is controversial. Some studies have recommended this treatment, while others reported it as ineffective and with considerable side effects. Therefore, these controversies highlight the need for further studies with higher comprehensiveness and accuracy. In addition, stem cells have helped the researchers illustrate the available ambiguities in the pathogenesis of the influenza virus, especially the relationship between influenza and some congenital abnormalities. Also, some studies have used stem cell models to identify the mechanisms involved in the pathogenesis and transmission of Zika and Ebola viruses. It is expected that these studies can be used in effective antiviral therapy developments against these pathogens.

Conclusion: The present study provides new insights into the effects of stem cells on emerging epidemic-prone diseases. Therefore, stem cell therapy can help us overcome challenges caused by these epidemic-prone diseases, such as re-emergence and functional ambiguities. Clinical trials during the COVID-19 pandemic have shown the potential benefits of stem cells and their derivatives in mortality reduction and recovery acceleration of the patients. It has been shown that stem cells can regulate immune responses, leading to reduced inflammation. Moreover, these cells play an effective role in tissue repair. Due to their differentiation ability, they are suitable for laboratory simulation. Thus, they can be essential tools for investigating the functions of Zika, Ebola, and Influenza viruses. Despite these promising findings, however, further studies are needed to evaluate the long-term effects and safety of this method. With recent advances, stem cells have revolutionized the medical sciences. These cells are expected to be an effective weapon for fighting microbial threats against the human population.

Keywords: Stem cell therapy, Cell therapy, Epidemic diseases, COVID-19

Therapeutic role of Cancer Testis Antigens in breast cancer: challenges and future perspectives (Review)

Motahareh Sheikh Hosseini,[1,*] Mohammad Moarefzadeh,[2] Mahdieh Salimi,[3]

1. Department of Medical Genetics, Institute of Medical Biotechnology, National Institute of Genetic Engineering and Biotechnology (NIGEB), Tehran, Iran.
2. Lorestan University of Medical Sciences, Lorestan, Iran.
3. Department of Medical Genetics, Institute of Medical Biotechnology, National Institute of Genetic Engineering and Biotechnology (NIGEB), Tehran, Iran.

Introduction: Breast cancer is the second leading cancer death and the most frequent cancer diagnosed among women across the world. Early diagnosis and effective screening play a significant role in reducing the mortality rate of breast cancer.

Methods: Since the heterogeneity of breast cancer causes a new challenge, there is no gold standard therapy proper for all tumors of the mammary gland. Therefore, it is important to distinguish novel therapeutic approaches such as applying tumor-associated molecules to target biomarkers. These targets enhance breast cancer screening. For this purpose, cancer-testis antigens (CTAs) have developed as powerful clinical biomarkers to target several malignancies due to their characteristics.

Results: CTAs are considered as tumor-associated antigens (TAAs) which demonstrate aberrant expression in several cancers including skin, ovaries, and breast. Furthermore, CTAs can be considered for early detection and therapeutic targets for cancer immunotherapy.

Conclusion: In the present study, the clinical implications of CTAs in breast cancer as biomarkers and immunotherapeutic targets and also a special focus on challenges and future perspectives have been discussed.

Keywords: Breast Cancer, Tumor Progression, Cancer Testis Antigens, Prognostic Biomarkers, Therapeutic Uses.

Three-dimensional spheroids as in vitro models for testing iron oxide nanoparticle-based drug delivery system: a review (Review)

Akram Ahvaraki,[1] Zeinab Bagheri,[2,*]

1. Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
2. Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran

Introduction: Cancer is the second leading cause of death worldwide and one of the diseases whose detection and treatment methods will soon undergo significant changes with the application of nanomedicine. Chemotherapy, along with surgery and radiation therapy, is one of the most common cancer treatments. For this reason, physicians and researchers have made significant efforts to optimize the drug's action and minimize side effects. The development of appropriate drug delivery systems represents a significant problem in cancer-targeted therapy. Various nanocarriers with exciting features have been demonstrated as the most effective carriers in this field. magnetic nanoparticles including Fe3O4 and γFe2O3 have outstanding biocompatibility and low toxicity. Thus, these two nano-oxides are extensively utilized in the targeted drug delivery, bioseparation, magnetic fluid hyperthermia, and magnetic resonance imaging. Recently, the three-dimensional spheroid tumor models have been recognized as an intermediate step between in vitro and in vivo models, increasing their biological relevance in research fields such as tumor biology and drug screening. Spheroids display a three-layered organization that containing proliferative, quiescent, and necrotic cells. The spheroid outer layer is made of highly proliferative cells with unrestricted access to oxygen and nutrients, and quiescent cells are found in the spheroid's middle layer, while necrotic cells are present in spheroids inner layer, being excluded of oxygen and nutrients. Due to spheroids' structural similarities with the in vivo solid tumors can be used to predict nanomedicines' tumoral penetration capacity and their optimal physicochemical properties.

Methods: The magnetic attributes of iron oxide nanoparticles (IONPs) depend on their composition and morphology. Thus, the synthetic method needs to be carefully selected, ensuring control over the particles' shape, size distribution, and crystallinity. IONPs can be produced in three different ways, encompassing chemical, physical, and biosynthetic methods. Chemical approaches are employed in the vast majority of cases. Physical methods, which include powder ball milling, electron beam lithography, aerosol, and gas-phase deposition, suffer from the lack of ability to control the size of particles in the nanometer size range. Biological methods rely on reduction-oxidation reactions, in which microbial enzymes or plant phytochemicals are

responsible for reducing salts into IONPs. However, the yield of such methods is low, and the size distribution is broad. For example, Hernández et.al. synthesized excellent IONPs for drug delivery application. They mixed iron (III) chloride hexahydrate with ammonia solution to produce a strong alkaline suspension. The size and shape of the nanoparticles can be controlled by modifying parameters such as temperature, pressure, and reaction time achieving sizes of 10–200 nm. Shen et al. developed a microemulsion method for synthesizing larger particles of IONPs that is a very critical feature in drug delivery application.

Results: Perez et al reported a method to reduce the maturation time required for cohesive spheroid formation.In this work, iron oxide nanoparticles conjugated with doxorubicin, average diameter 8 nm, were produced by an iron salt coprecipitation. The relationship between spheroid size and spheroid maturation was measured to demonstrate the application of these spheroids in drug screening and toxicity assessments. In other research, Don N. Ho et al, reported a 3D platform was designed to study the penetration of nanoparticles into tumors that tested with a model NP, tumstatin-Fe3O4 NPs. Their results showed that tumstatin-Fe3O4 NPs could specifically target the endothelial cells in a complex 3D microtissue environment. To determine the effects of free and SPION-bound paclitaxel (Ptx) in 3D cell culture, Luget et al, reported 2D and 3D cell culture experiments suggested that SPIONLA-HSA-Ptx is a potential system for magnetically based targeted drug delivery to different breast cancer tumors.

Conclusion: Fe3O4 NPs are one of the most widely used NPs that are clinically safe and able to act as therapeutics in cancer therapy. also, tumor spheroids that mimic the solid tumor properties, are considered to be a significant platform to evaluate the delivery of anticancer drugs.

Keywords: magnetic nanoparticles,nanomedicine,drug delivery,spheroid,cancer

Tissue engineering and Stem Cell (Review)

Amirmohammad Ghazanfari,[1,*]

1. Imam Ali Guidance School

Introduction: When tissues or organs have been so seriously unhealthy or lost by cancer, inborn unusualness, or damaged that usual medical treatments are no more suitable, dummy organs (including tissues) or organ transplantation are the first selection to reconstruct the destroyed tissues or organs. However, todays, these surgical remedies have been facing a number of disagreements with. Artificial organs have been improved by wonderful improvements in the biomedical engineering in the past decades, but however they need better biocompatibility and bio functionality. Worries in current organ transplantation consist lack of forgiven organs and immune rejection, although immunosuppressive treatment has recently much up to date.

Methods: As pointed above, the cell, growth and scaffold factor are the three main materials for tissue engineering. The cell combines matrices of young tissue, while the scaffold affords the suitable environment for cells to be able to effectively complete their duties. The mission of growth factors is to help and increase cells to remake new tissue. Although many researches have been undertaken to regenerate various kinds of tissue, there are still a lot of critical factors contains in this regenerative schedule, containing, scaffold construction, cell source, cell seeding, matrix production analysis, culture environment, mechanical properties of cell–scaffold construct and reasonable animal models. However, it may be possible sometime in the future to separate unhealthy cells by means of a partial biopsy, increase the cell amount in the culture, seed cells onto a three-dimensional scaffold and implant to the similar patient.

Results: Scaffold-based tissue engineering using stem cells has progressed the area of tissue reformation in medicine; Anyway, it is still at the exiguity level. A wide in-depth scientific information and study of various stem cells will go a long path to convert them to clinical use. Furthermore, rather extra studies are required to be accomplished on various scaffold plans because the achievement of tissue engineering belongs on these scaffolds and enables a niche to transplanted cells. In addition, most of the usage of stem cells in tissue regeneration has been guided toward small tissue illness as such tries to expand bioengineered grafts to remedy larger tissue defects (bone defects) should be made. So many stem cells like induced pluripotent stem cell, mesenchymal stem cells, and ASCs are promising source of patient-specific stem cells with great regenerative potential. However, few or no clinical translation is available as they are potential teratoma and carcinogenic causative agents, and avoidance of certain of these cells is

supposed unethical. Anyway, more clinical considerations are demanded to be suitably certain they are secure clinically

Conclusion: However, Scaffold-based bone tissue engineering using stem cells is at its minority. A deep scientific information of each special stem cell type is essential to recognize how to convert them to clinic, which may enforce completely modern practices. So, the opinion of using heterogeneous cell sources (e.g., adipose and bone marrow tissues) that do not need in vitro culture might affect in stronger influence. This is individually considerable as stem cells appear to have mechanical memory and save knowledge from previous physical environments, which can affect the cell chance. Overcoming the mass conveyor restriction for a bioengineered bone graft will clear the way to the cure of rough bone weakness. Contemporary tissue engineering cures are often aimed for partly small defects and are unskilled contrasted to native tissue. Altogether, there are many barriers on the way for the remedy of old degenerative sicknesses and in regenerative cure using MSCs. Some of the other existing challenges contain guaranteeing the long-term modality of mending and avoiding potential side results of cure such as carcinogenesis.

Keywords: tissue engineering, disease, stem cell, scaffold

Tissue engineering in the vascular system (Review)

Elham Zendedel,[1,*] Shiva Asadpour,[2]

1. Department of Tissue Engineering and Applied Cell Sciences, School of Advanced Technologies, Shahrekord University of Medical Sciences, Shahrekord, Iran
2. Department of Tissue Engineering and Applied Cell Sciences, School of Advanced Technologies, Shahrekord University of Medical Sciences, Shahrekord, Iran

Introduction: The prevalence of cardiovascular illnesses, as well as a scarcity of suitable autologous tissues, has prompted and accelerated the development of tissue-engineered vascular grafts (TEVGs). Vascular tissue engineering has the potential to have a substantial influence on a wide range of clinical issues. Despite significant research into synthetic polymers as vascular engineering alternatives, they fall short of solving the biological difficulties at the blood–material interface. To overcome these problems and improve the long-term patency of vascular grafts, several tissue engineering methods have developed. The seeding of vascular cells onto scaffolds and the development of bioactive polymers for in situ arterial regeneration have both shown promising outcomes. The difficulties in developing engineered constructs that meet the physiologic, immunologic, and manufacturing requirements of engineered vasculature will be discussed.

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Conclusion: The difficulties in developing engineered constructs that meet the physiologic, immunologic, and manufacturing requirements of engineered vasculature will be discussed.

Keywords: Tissue engineering, Bioactive polymers, cardiovascular illnesses

Title: Leukoreduction Filters; a New Source of Microparticle for Human and Animal Study (Review)

Mohammad Reza Javan,[1,*] Sahar balagholi,[2] Sedigheh Amini Kafi-Abad,[3] samira karami,[4] Rasol dabbaghi,[5]

1. Blood Transfusion Research Center, High Institute for Research and Education in transfusion Medicine, Tehran, Iran.
2. Blood Transfusion Research Center, High Institute for Research and Education in transfusion Medicine, Tehran, Iran.
3. Blood Transfusion Research Center, High Institute for Research and Education in transfusion Medicine, Tehran, Iran.
4. Hematopoietic Stem Cell Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
5. Department of Hematology, Faculty of Medical sciences, Tarbiat Modares University, Tehran, Iran

Introduction: The isolation of microparticle from leukoreduction filters (LRFs) during cell extraction process can be introduced LRFs as precious source of Microparticle for animal and human study.

Methods: 10BioR blood filters were collected from Tehran Blood Transfusion Center. Back-flushing method was used for microparticle isolation from the LRFs. Dynamic light scattering (DLS), electron microscopy (EM), and flowcytomerty were performed for evaluation of microparticle size, Morphology, and structural properties respectively. Statistical analyses were carried out for evaluation of different between test and control groups. a p value of less than 0.05 indicates that a difference is significant.

Results: DLS analysis showed that the average microparticle size in the test and control samples was 235.7 nm and 189.5 nm respectively. We were able to separate 1202095.34 and 280948.64 microparticles from each test and control samples, respectively and the difference was significant (p value<0.008). We proved that the count of CD41, CD14, CD34 and CD235a microparticles in tests sample were 348213, 271378.4, 21464.6 and 57864.9 respectively while in control samples CD41, CD14, CD34 and CD235a microparticle count were 59246.2, 24167.6, 3033.2 and 96526.8 respectively. Statistical analysis showed the significant difference between the count of only CD14 and CD41 microparticles between test and control samples (p value<0.008). SEM showed that spherical, oval, cell fragment and micro-aggregate shapes while TEM revealed mitochondrial body in the samples.

Conclusion: It is concluded that LRFs, which until now were considered as blood transfusion waste, can be a source for extracting a large volume of cells

microparticles with different structural properties for animal and human phase studies.

Keywords: Back-flushing; Microparticle; Leukoreduction filter

Tracking of carcinoembryonic antigen in early stages of colorectal cancer by graphene quantum dots-Based electrochemical immunosensor and aptasensor (Review)

Safoora Mohammadzadeh,[1] Mohammad Hassan Emami,[2] Samane Mohammadzadeh,[3] Fatemeh Maghool,[4] -,[5] -,[6,*]

1. Poursina Hakim Digestive Diseases Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
2. Poursina Hakim Digestive Diseases Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
3.
4. Poursina Hakim Digestive Diseases Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
5.
6.

Introduction: Carcinoembryonic antigen (CEA) is one of the most widespread colorectal cancers (CRC) biomarker. However, this antigen has low concentration in early stages of CRC, which could not be detected by common methods. In this review, we discuss the sensitive method for detection of CEA in the early stage of CRC. Electrochemical method as a high sensitivity, rapid response, easy to use and low-cost method, could be useful for detection of low levels of CEA. Different types of nanomaterials such as quantum dots and nanoparticles have been used on support materials to achieve high conductivity and boost detection signal in electrochemical sensors. Graphene quantum dots (GQDs) because of high mobility of charge carriers, chemical inertness, low toxicity, large specific surface area, and attractive biocompatibility have great potential applications in electrochemical detection. High specific interaction of antigen-antibody in electrochemical immunosensors and high affinity and specificity of electrochemical aptasensors provide the specific analysis of CEA. In this review has been shown that physical-chemical properties of GQDs and GQDs composites improve sensitivity of electrochemical immunosensors and aptasensors signals for determination of CEA

Methods: Relevant English published studies were included in this review.

Results: N, S-graphene quantum dots@Au-polyaniline impedimetric immunosensor could be applied for the selective detection of CEA in the linear range of 0.5–1000 ng/mL with good limit of detection (LOD) of 0.01 ng/mL. In addition, quantitative detection of CEA has been achieved with nitrogen-doped graphene quantum dots/ PtPd bimetallic nanoparticles/ Au nanoparticles immunosensor. The antibody-conjugated nanocomposite intensify the sensitivity of electrochemical signal in broad dynamic range, with

a LOD of 2 fg/mL for the detection of CEA. Furthermore, sensitive electrochemical aptasensor based on graphene quantum dots ionic liquid nafion nanomatrix has been reported for the determination of CEA concentrations. Electrochemical signals of aptasensor in presence of CEA have improved and exhibited the best detection limit of 0.34 fg/mL. The quantitative determination of CEA was achieved with the best linear response in the 10.0 fg/mL to 200.0 ng/mL CEA concentration using sandwich type GQDs/Au/graphene aptasensor. Signal amplification of CEA sensing has been obtained by new constructed sandwich sensing platform is from linkage of CEA aptamer to hemin–G–quadruplex DNAzyme

Conclusion: Immunosensors and aptasensors based on graphene-quantom dots composites with broad linear range for detection of CEA could be applied for the detection of CEA in the early stages of CRC.

Keywords: Carcinoembryonic antigen, Graphene quantum dots, Electrochemical, Immunosensor, Aptasensor

Treatment Failure in Acute Myeloid Leukemia: Focus on the Role of Extracellular Vesicles (Review)

Majid Gholizadeh,[1] Leila Noorazar,[2] Mozhdeh Mohammadian,[3] Abbas Hajifathali,[4] Ghazaleh Sankanian,[5] Elham Roshandel,[6,*]

1. 1Department of Hematology and Blood Banking, School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran / 2Hematopoietic Stem Cell Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
2. 1Department of Hematology and Blood Banking, School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran / 2Hematopoietic Stem Cell Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
3. Hematopoietic Stem Cell Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
4. Hematopoietic Stem Cell Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
5. Hematopoietic Stem Cell Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
6. Hematopoietic Stem Cell Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Introduction: Acute myeloblastic leukemia (AML) is one of the most common types of blood malignancies that results in an AML-associated high mortality rate each year. Several causes have been reported as predisposing factors for AML in children and adults, the most important of which are cytogenetic abnormalities and environmental risk factors. Following the discovery of numerous drugs for AML treatment, leukemic cells sought a way to escape from the cytotoxic effects of chemotherapy drugs, leading to treatment failure. Nowadays, comprehensive studies have looked at the role of Extracellular Vesicles (EVs) secreted by AML blasts and how the microenvironment of the tumor changes in favor of cancer progression and survival to discover the mechanisms of treatment failure to choose the well-advised treatment. In this study, we aim to review the mechanisms that protect the leukemic cells from chemotherapy agents and the roles of leukemia-derived EVs in the induction of drug resistance.

Methods: Collecting related articles was performed by Searching keywords including “Acute Myeloblastic Leukemia”, “Drug Resistance”, “Treatment Failure”, “Extracellular Vesicle”, in several databases such as https://scholar.google.com/, https://pubmed.ncbi.nlm.nih.gov/, https://www.scopus.com/. At the next step, similar items were removed and selected articles were classified based on desired sub-titles.

Results: Reports showed that malignant cells secrete EVs that transmit messages to adjacent cells and the tumor's microenvironment. Also, increased secretion of EVs in various malignancies indicates an unfavorable prognostic factor and the possibility of drug resistance. EVs play a potent role in the protection of malignant cells in several ways including transferring of immunosuppressive molecules, microRNA, and organelles by EVs. Also changing in BCL2 family proteins via regulatory factors content in EVs can increase survival of leukemic cells that lead to escape cells from death and result in treatment failure.

Conclusion: Numerous studies have highlighted the undeniable role of extracellular vehicles (EVs) in cell-cell communication. Accordingly, EVs can alter the function of target cells by transferring the contents of their origin cell. Recent researches underscore the role of EVs in cancer drug resistance. In this study, we briefly reviewed the challenges of treating AML with a glance at the EVs' role in this process. It is hoped that with a deeper understanding of EVs, new therapies will be developed to eliminate the relapse of leukemic cells.

Keywords: Acute Myeloblastic Leukemia, Drug Resistance, Treatment Failure, Extracellular Vesicle

Treatment of cancer with the help of exosomes (Research Paper)

HOSSEIN AMERI SHAHRABI,[1,*] HOSSEIN SAYAF,[2] Mohammadreza Forouharmanesh,[3]

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Introduction: Cancer begins and spreads with the uncontrolled growth of cells in the body. This is a simpler definition of cancer Be that: The abnormal growth of the body's cells begins by ignoring the normal rules of cell division of the body. Normal cells of the body are constantly on Now they are producing signals that indicate whether this cell should divide or differentiate into another cell or its lifespan. The cell is finished or not. But do cancer cells pay attention to these signals or do they produce them themselves? Which causes abnormal growth of cells and causes cancer] 1 Long unencrypted A (lncRNAs) play an important role in tumor progression and are suddenly expressed in various cancers. To be. However, the functional role of lncRNAs in breast cancer remains largely unknown [16]. Traditional methods of treating cancer, including radiotherapy, chemotherapy, and immunotherapy, all have their own limitations. An approach New is bacterial therapy, either used alone, or in combination with conventional methods, has a positive effect on tumor regression and inhibition It has metastasized. Targeted treatment of the tumor with the help of bacteria, which is used as a therapeutic / gene / drug vehicle, is very promising. 7 In the treatment of tumors. It was found that the use of bacteria or in combination with conventional methods in some experimental models of cancer (regression) Tumor and increase survival (effective] 17.] Research on bacterial toxins is closely linked to the birth of immunology. Our understanding of the interaction of bacterial protein toxin with immune cells To decipher the immunological pathology, to develop preventive and curative treatments for infections, and to suggest anti-cancer immunotherapy methods. Helps. More recently, immunotoxins have been used to kill cancer cells targeted by specific antibodies or cytokines. Have been designed and used [18] Tumor microenvironment (TME) has the ability to act as a stimulant for breast cancer progression and metastasis. TME of stromal cells Extracellular matrix and soluble c-tokens, chemokines and extracellular vesicles and nanoparticles are formed that actively affect Affects cell activity. Extracellular vesicles contain large exosomes, microcycles, and oncosomes that develop during tumor progression. They regulate basic processes by interacting directly with target cells. Breast cancer exosomes by angiogenesis, invasion of the system Strengthen immunity and resistance to chemotherapy and metastasis to the tumor. Exosomes in almost all physiological fluids, including plasma, Urine, saliva and breast milk are found and provide a valuable source for the development of non-invasive cancer biomarkers [19].] Chronic

inflammation is associated with the presence of foam cells in many infectious and metabolic diseases and some cancers. These cells form when The intracellular fat content of macrophages exceeds their capacity to maintain homeostasis. Decreased vital macrophage safety functions Finds. Patterns of foam cell formation are caused by atherosclerosis. Recent studies show that the mechanisms of foam cell biogenesis in The length of tuberculosis differs from that of those working during atherogenesis [20]. Worldwide, breast cancer is one of the leading causes of premature death and death in women. In the United States, breast cancer is more prevalent than anywhere else Other than lung cancer, it can lead to cancer death in women. Various factors for breast cancer are found through epidemiological studies It includes race, ethnicity, family history of cancer, genetic characteristics as well as alcohol use, physical inactivity, Exogenous hormones have been shown in some women. Reproductive factors such as younger age at pregnancy and older age at first complete pregnancy can Through long-term effects on the level of sex hormones or other biological mechanisms affect the risk of breast cancer. Cancer Triple negative breasts may have a specific cause. Genetic types and mutations in genes that make proteins that are in the pathways DNA repair is involved and a homologous combination of double-stranded interrupts (APEX1 DNA, BRCA1, BRCA2, XRCC2, XRCC3 ATM, CHEK2, PALB2, RAD51, XPD,) is involved in some cases of breast cancer [21.] Tumor-associated macrophages (TAMs) aerobic glycolysis and apoptotic resistance of breast cancer cells through extracellular vesicle transfer EV) increase the translocation of a specific myeloid lncRNA, 1α-HIF RNA stabilizer without longitudinal encoding (HISLA). In terms of Mechanically, HISLA blocks the interaction of PHD2 and 1α-HIF to inhibit hydroxylation and degradation of 1α-HIF. Electate released from Glycolytic tumor cells rearrange HISLA in macrophages and form a feeding link between TAM and tumor cells gives . Blocking HISLA transmitted by EV inhibits glycolysis and chemical resistance of breast cancer in vivo. From Clinically, HISLA expression in TAMs is associated with glycolysis, poor chemotherapy response and shorter survival in breast cancer patients Is. Our study examines the potential of lncRNAs as signal transducers between immune cells and tumors via electrical transmitters Transmitted to enhance cancerous aerobic glycolysis [22] The role of some bacterial toxins in inhibiting cancer cell proliferation has been identified. The most well-known function of the toxin Botulinum has its effects on cell integrity and cell skeleton. In 2013, Bandala and colleagues discovered the effect of Botulinum toxin Showed proliferation and apoptosis of T47D cancer cells. They indicated that Botulinum treatment may be an alternative Be considered as a common treatment for breast cancer. However the molecular pathways induced by Botulinum which Its cytotoxic activity is effective. Not well identified. Delivery Efficacy of miRNA mimics and / or antagonists to tumor cells is a major challenge in treatment-based miRNA is cancer. Current Approach to Delivery of Gene-Based Therapies and RNAi-Based Therapies It is a viral or non-viral carrier system. Methods that directly

utilize viral vectors cause transmission They become efficient genes, although sometimes they have inefficiencies. Limitations on the use of the viral approach to gene transfer And recombinogenic 2, cytopathic 3 associated with defects in tumor targeting and residual viral elements that can be immunogenic 4 Be) 24.) The use of non-viral vectors in gene transfer may not have some of the problems associated with non-viral vectors. In this Significant advances in the development of pharmaceutical formulations and non-viral systems for in vivo in gene therapy It has been found that in particular, gene transfer systems due to cationic liposomes can be mentioned. Cationic liposomes They consist of two positively charged lipid layers and can be exposed to naked DNA, which is negatively charged, by simple lipid mixing. And DNA complexes, so that the resulting complex (lipoplex) 5 (Has an overall positive charge) 20.) Lipoplex easily It is attached to the cell and is absorbed by the cell with high transfection efficiency. The properties of cationic liposomes that make them for DNA delivery is attractive and adaptable. The following can be mentioned: • Ease of preparation; • Ability to form complexes with large amounts of DNA; • Practical adaptability to any type and size of DNA or RNA; • Ability to transfect different types of cells, including indivisible cells; • Lack of immunogenicity Or inactivity biohazard 6 7 .) 25, 24 (Currently, several clinical trials are underway using cationic liposomes to deliver genes. Also liposomes for delivery of chemotherapeutic agents such as Doxorubicin for breast cancer chemotherapy already 8 There is an important drawback to the use of cationic liposomes is that they lack tumor specificity. Are and in proportion They have low transfection efficiency compared to viral vectors. However, the tumor specificity of lipoplexes can be carried by ligand transport 9, which is detected by the cell surface receptor, increases dramatically. Receptor-mediated endocytosis Cell entry path Highly efficient in eukaryotic cells. Ligand placement on lipoplex prevents DNA from entering cells through initial binding The ligand facilitates the cell surface receptor and subsequent entry of the attached lipoplex into the cell. Upon entering the cell, DNA It goes out of the endocytosis pathway to be expressed in the cell nucleus (24, 25). In order to effectively deliver DNA to the cell, tumor-specific DNA-nanoparticle lipoplex systems with ligand targeting capabilities and Developed for cancer gene therapy) US patent number: 6749863 and European patent number: 10 self-assembly Or scFv against transferrin receptor 11 1154756 EP [) 26, 27.] These nano-transport systems, transferrin In the case of cancers 12 [22, 23] using transferrin are overexpressed as 13 humans, as a targeted ligand for the tumor A target ligand, Xu et al. [26] Self-assembled nanocarriers in 50 to 90 nm sizes with a They were new and obtained like a viral particle with 14 densities and a desirable surface load. These nanocarriers have nanostructures They are dense centers surrounded by a membrane covered with transferrin molecules on the surface. This nano-carrier system is efficient and To cancer cells in 15 promising properties for targeted delivery of antisense genes and oligonucleotides Shown in vivo environment [28.] One of the most

controversial topics in the field of nanobiotechnology is the introduction of an efficient, safe and secure carrier for drug and gene transfer to tissues. Is the goal. So far, various nanocarriers of polymer, fat, protein, polysaccharide, metal, etc. have been introduced for the purpose that each Which, either due to toxicity or low absorption in human cells or rapid clearance by the immune system, is very efficient in transmission They lacked drugs and genes, and this effort continues among researchers to introduce more efficient systems. Nanoparticles used To transmit drugs and genes, they must be stable, biocompatible, biodegradable, non-inflammatory, non-toxic. Also the ability to escape from Have a reticuloendothelial system so that they can circulate longer in the blood. One of the important features of targeting ability Is a specific and successful target cell or tissue that, if a carrier has such a property, has a high score and rank among carriers. Will no longer enjoy. Virus-derived structures have long been considered one of the most efficient drug and gene carriers. However, due to their immunogenicity and the potential risk to them, the importance of these natural nanocarriers for systems Transfer was reduced and researchers turned to synthetic structures such as metal nanoparticles and polymers. Gradually the toxicity of these structures It also prevented the development of these systems and their therapeutic use (29, 30). Today, researchers believe that this goal can be achieved only by modeling the biological structures in the human body. One These biological nanostructures that play their role efficiently in the transfer of macromolecules and nucleic acids between cells Are exosomes. These natural nanowicels in the human body are responsible for the transport of proteins, RNAs, and in some cases DNA. It is responsible from one cell to another. They are completely stable, as reported after 6 months of purification and maintenance They have not undergone any change in their structure. Because it is found in all body fluids, it is completely non-immunogenic They will go and will not carry the risk of pathogenicity that viral vectors had. Most important of all exosomes because through fusion And membrane integration, transport their cargo directly to the cell cytosol, thus preventing them from invading and clearing the environment. They retain cells and do not engage in the process of escaping the endosomal structure (31). Katakowski et al. Exosomes secreted by mesenchymal stem cells were used to load 146b-Mir. This method of miRNA treatment using xerosomes can effectively prevent tumor growth. In addition to siRNAs and 10 Self-assembled 11 Transfer 12 Transfer receptor 13 Tumor-targeting ligand 14 Nanostructure 15 Anti-sense oligonucleotide 10 miRNAs, mRNAs can also be transported by exosomes as a commodity. (32) Recently secreted in HEK-293; Inhibited DNA synthesis in mice and improved tumor cell apoptosis. 33) Exosomes can also be types Load other drugs as well. Example In 2013, Zhuang and colleagues found that curcumin in lymphocyte exosomes Loaded mice can be successfully transferred to brain tissue and improve the apoptosis of microglia cells in the brain. results Their work suggests that this strategy may provide a new non-invasive and therapeutic approach to treating inflammatory brain diseases.

34) There are also other studies on the effect of genetic content of exosomes in the treatment of cancer, all of which confirm its effectiveness. Exosomes are involved in gene transfer (35, 36).

Methods: 1- Separation of extracellular microvesicles from cells derived from breast carcinoma: based on centrifuge protocol Differential and Quick Exo extraction extraction separation kit is performed by Biosciences System Company. 2 - Confirmation of the accuracy of extraterrestrial microuricles isolated in terms of size and morphology by electron microscopy: For microscopic observation, a small volume of purified exosome is fixed with 2.5% glutaraldehyde and washed with PBS. The sample is then dewatered with ethanol on a dry glass surface and covered with a thin layer of gold. Size and morphology Exosomes are evaluated by electron microscopy. 3- Evaluation of HOTAIR oncogene expression in tumor microvesicles: RNA extraction: In order to extract RNA in this study from Trizol (Invitrogen) was used. Trizol solution formed RNA complexes with 16 reactant molecules. It is guanidinium and water, but prevents the hydrophilic binding of RNA to DNA and proteins. Then DNA and proteins They are separated from the aqueous phase while the RNA molecules remain in this part. 4-Synthesis of cDNA from samples using TAKARA kit and study of HOTAIR expression by time-Real PCR 5- Preparation of 231-MB-MDA breast cancer grade from Iran Sastor Institute 6 - Evaluation of cytotoxicity of bacterial enzyme toxin A Cytolysin (Sigma Company) on the breast cancer strain 231-MB-MDA by assay MTT It will be 17 micrograms per fruit to calculate the optimal dose and IC50. MTT test to evaluate cell proliferation Then It is treated with an external agent. The basis of this technique is based on reduction of MTT yellow substrate to purple sediment By the enzyme mitochondrial dehydrogenase succinate in living cells. Dye intensity produced after dissolving 18 formazan Formazan deposition in organic conditions such as dimethyl sulfoxide can be measured by spectrophotometry And is directly related to the number of living cells and cell proliferation. 7- Loading of toxin (Sigma Company) into extracellular vesicles by sonication / incubation method 8- Treatment of breast cancer cells 231-MB-MDA in the following groups: 1- Cell group treated with foreign vesicles Cell 2 - Toxin-treated cell group 3) Cell group with extracellular vesicles containing toxin 4) Control cell group -9 16 Reagent 17 Cell proliferation 18 Formazan 14 10-Study of expression of transcripts of asostosis-related genes (2-BCL and BAX) by time-Real PCR (Housekepping gene: GAPDH:) Time-Real PCR technique based on quantitative measurement of amplified product during the exponential phase of PCR reaction from The way to measure the amount of light emitted is fluorescence. As the meaning of the word implies, the concept of time-real PCR is observed Moment by moment is the process of reproduction. In this diagnostic system, a fluorescent material that can be measured is used it is possible. During the reaction, this fluorescent dye emits fluorescent light in proportion to the amount of products produced from each cycle and the amount Its

fluorescence emission is detected and recorded by the device indicator. Time-Real PCR for target and reference genes Is determined. In the following, 19 examples are performed. At the end of the multiplication and based on the drawn diagram, the threshold cycle After calculating the difference between the mean CT of the reference gene and the mean CT of the target gene for both control and test samples, the ΔCT index in two A sample of control and testing is obtained. Also, from the difference between the two ΔCTs, an index called ΔΔCT is calculated. 11 - Focytometric evaluation of treated cells in the above groups 12-Data analysis

Results: Exosomes are a good tool because they only grow and are secreted into cancer cells, so that we can send the title of therapeutic drugs to cancer cells with the help of these exosomes and make treatment easier and make it possible for It allows us not to damage the rest of the Bern cells

Conclusion: Our research needs further investigation and testing. To reach the effectiveness and treatment of NP

Keywords: Xezosome - Cancer - Treatment -

Treatment of diseases of the nervous system by stem cells (Review)

Mobina Ashooi,[1,*]

1. Ibn Yamin High School

Introduction: Stem cells are cells that have the ability to differentiate into cell types, including embryonic cells, adult stem cells, and cord blood stem cells, and have unique characteristics. Their first characteristic is reproducibility, their second characteristic is the nature of non-differentiation, and their third characteristic is their ability to differentiate into cells of different tissues. The most important uses of stem cells include repairing damaged tissues and bone tissue, treating cancer, treating diseases and nerve and spinal cord injuries, repairing burns, treating diabetes, treating infertility and others. Stem cells are a good source for treating neurological diseases.

Methods: A variety of neurological diseases and treatment by stem cells A: Epilepsy: According to a new study from Belarus University of Medical Sciences: Mesenchymal stem cells have been developed to compensate for the limited efficacy of antiepileptic drugs, which are unresponsive in many patients, so in order to test this hypothesis, researchers Intravenous injections also treated mesenchymal stem cells. The results of the evaluations showed that the patients who received cell therapy with antiepileptic drugs achieved a 30% improvement and did not experience any seizures for a year while these patients were monitored and did not have any side effects. was not observed. B: Alzheimer's and cell therapy So far, studies have been conducted on various sources of stem cells in this field. Transplanted mesenchymal stem cells in the brains of Alzheimer's mice become mature cells and improve memory and learning. It should be noted that the use of stem cells in the treatment of Alzheimer's disease requires further research because in this disease, nerve cells in different areas of the brain are damaged and the exact mechanisms of this disease are not yet fully understood. A: Multiple sclerosis Stem cell transplantation from any cell source can be a safe and effective treatment for it, however, since there is no controlled study compared to stem cell therapy, finding a reliable answer about the safety and efficacy of this type. Treatment for patients with MS requires comprehensive research in the future with a large group of patients. D: Parkinson Stem cells including mesenchymal stem cells, embryonic cells and nerve stem cells are considered as suitable and practical alternatives for the treatment and control of Parkinson's. In a clinical trial conducted in Turkey in 2016, 21 patients aged 42 to 79 years with Parkinson's disease were treated using neural stem cells extracted from the fetal brain by one-way injection of striatum at regular intervals. Significant improvement in motor function without side effects. R: Stroke Cell therapy can be an alternative intervention to change the treatment method. Different cells are considered as a suitable option for cell therapy. In

basic science studies on ischemic stroke, cell injection has shown different results. Satisfactory results of basic science studies have been used in phase one and two clinical studies. Almost the majority of these studies have emphasized the safety and reproducibility of cell use. .

Results: Since the risk of disease recovery and success rate with drug therapy is low in neurological and spinal cord injuries, stem cell therapy can be used as a new method in the treatment of such diseases. Also in this area, attention should be paid to the ethical problems and safety of stem cell use. In addition, the long-term safety of stem cell transplantation is still an unanswered question.

Conclusion: Cell therapy for the treatment of neurodegenerative disorders is in its early stages and still has room for improvement. There are many fundamental issues that need to be addressed. For example, recognizing the molecular properties of stem cell proliferation to cause genetic modification is one of the concerns today. In addition, in order to develop the use of stem cells in diseases, laboratory studies should also be performed on models of neurological disorders that fully reflect the symptoms of the disease in humans. Such models identify the potential benefits and risks of using stem cells in humans before using them in the clinic. It is worth noting that achieving a suitable cell therapy method in the clinical field requires a lot of time and effort, which in itself should not diminish our enthusiasm to achieve this goal.

Keywords: Application of stem cells, Neurological diseases

Trifolium pratense L. (Red Clover) Extract and Doxorubicin Synergistically Inhibits Proliferation of 4T1 Breast Cancer in Tumor-Bearing BALB/c Mice Through Modulation of Apoptosis and Increase Anti-Oxidant and Anti-Inflammatory Related Pathways (Research Paper)

Mohsen Akbaribazm ,[1,*]

1. Fertility and Infertility Research Center, Health Technology Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran

Introduction: Therapeutic strategies against triple negative breast cancer (TNBC) are associated with drug-induced toxicities. Trifolium pratense L. (T. pratense) is rich in polyphenolic compounds which confer the plant potential anti-cancer properties. The aim of this study was to investigate the effects of T. pratense and doxorubicin (DOX) on the apoptosis and proliferation of 4T1 tumor cells in an allograft model of tumor-bearing BALB/c mice.

Methods: Fifty-six female 4T1-tumor bearing-BALB/c mice were randomly divided into 7 groups (n=8/group) to receive different doses and combinations of DOX and T. pratense extract for 35 days. On the 36th day, serum estradiol (E2), IL-12 and IFN-γ cytokines, and glutathione peroxidase (GPx) activity were measured. Tumor's ferric reducing antioxidant power (FRAP) and the expressions of apoptosis-related genes (p53, Bax, Bcl-2, and caspase-3) were also evaluated. Immunohistochemically staining for Ki-67 and p53 were performed.

Results: Our results showed that the co-treatment of DOX and T. pratense (100–400 mg/kg) inhibited the proliferation of 4T1 tumor cells in dose- and time-dependent manners by decreasing the serum level of E2 (as a stimulant for breast tumor growth) and increasing the serum levels of IL-12 and IFN-γ along with significant increments in serum GPx and tumor FRAP activities. The co-administration of DOX and T. pratense also decreased the expression of Ki-67 proliferation marker and increased the number p-53 positive (i.e. apoptotic) cells within tumors. This was accompanied with the upregulation of pro-apoptotic and down-regulation of anti-apoptotic genes.

Conclusion: The key findings indicated the synergistic effects of DOX and T. pretense against TNBC xenografts.

Keywords: Trifolium pratense L., Apoptosis, Breast cancer, Doxorubicin, 4T1 cell.

Tumor viruses, Oncogenesis and human cancers: Host-Virus interactions (Review)

Piruz Shadbash,[1] Seyed Reza Mohebbi,[2,*] Seyed Masoud Hosseini,[3] Seyed Amirmohammad Seyed Mirzajani,[4] Shabnam Kazemian,[5] Hamid Asadzadeh-Aghdaei,[6]

1. Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences
2. Research Center for Gastroenterology and Liver Diseases, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
4. Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences
5. Research Center for Gastroenterology and Liver Diseases, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
6. Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Introduction: Tumor viruses or oncogenic viruses are viral agents capable of causing cancer. Since the first understanding of Retroviruses in the 1950-1960s, the term of Oncoviruses has been used to indicate the characteristics of these RNA viruses. The main viruses related to human cancers are the human papillomavirus (HPV), the hepatitis B and hepatitis C viruses (HBV and HCV), the Epstein-Barr virus (EBV), the human T-lymphotropic virus (HTLV), the Kaposi sarcoma-related herpesvirus (KSHV) and Merkel cell polyomavirus (MCPyV).

Methods: They seem to be the second most important risk factor for cancer development in humans. It seems that the majority of human and animal viruses do not cause cancer, likely due to the long-term evolution between the virus and its host. Studying the Oncoviruses is crucial for a better understanding of cell cycle control mechanisms and relevant host genes such as retinoblastoma.

Results: In 2002, the world health organization International Agency for Research on Cancer estimated that infections stimulated around 17% of human cancers, from this about 11.9% caused by one of these seven viruses.

A recent study of 2658 samples from 38 different types of cancers has revealed that 16% of cancers possibly originated from a virus.

Conclusion: These cancers can be prevented via vaccination, precise screening, on-time diagnosis using proper tests, and treatment. Mechanisms of viral carcinogenesis consist of generating genomic instability, increasing the rate of uncontrolled cell proliferation, resistance to apoptosis, constant inflammation, alterations in DNA repair mechanisms, and alteration of cell polarity, which often coexist with evasion mechanisms of the antiviral immune response.

Keywords: Tumor viruses, Oncogenesis, Long- term evolution, genomic instability, constant inflammation

Two layered nanofibrous mat with grape seed extract can promote wound healing in diabetic rat (Research Paper)

fereshteh nejaddehbashi,[1,*] zeinab rafiee,[2] mahmoud orazizadeh,[3] vahid bayati,[4] Ali asghar Hemmati,[5] Mahmoud hashemitabar,[6]

1. Cellular and Molecular Research Center, Medical Basic Sciences Research Institute, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
2.
3. Cellular and Molecular Research Center, Medical Basic Sciences Research Institute,Department of Anatomical Sciences, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
4. Cellular and Molecular Research Center, Medical Basic Sciences Research Institute,Department of Anatomical Sciences, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
5. Medicinal Plant Research Center, School of pharmacy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
6. Cellular and Molecular Research Center, Medical Basic Sciences Research Institute,Department of Anatomical Sciences, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Introduction: Background:Despite special advances in regenerative medicine, wound healing is a challenging medical problem. The skin is the largest organ in the human body that has essential and important functions, so any damage to its normal structure should be treated as soon as possible.

Methods: Materials and methods: In this study PCL/SSD, PCL/Coll as two - layered nanofibrous mat were designed with electrospinning. In vitro tests including FE-SEM, Release test, MTT assay and EDX test were done and in vitro evaluation for their healing ability in a diabetic rat model of a full-thickness excisional wound was done. Post operation study including H&E and trichromasons were done on parrafine sections after 3, 7 and 10 days after transplantation The healing process was evaluated with macroscopic observation on 3,7 and 14 days' post wounding. Hematoxylin - Eosin and Trichromasons staining was done to evaluate tissue remodeling and collagen synthesis

Results: Results: This combination of nanofibrous mat with grape extract showed appropriate normal characteristics with desirable skin wound healing. Moreover, attachment and spreading of limbal stem cells on this nanofibrous composite was reported to be in an optimal condition. As well, in vivo evaluation demonstrated that full repaired skin had been observed on day 14 in the two-layered nanofibrous mat with grape extract group after being wounded.

Conclusion: Conclusion: The two-layered nanofibrous mat with grape extract could be considered as a suitable wound dressing of nanofibrous membranes in future in order to shorten healing time.

Keywords: Key words:grape seed extract,nanofibrous mat,electrospinning,diabetic rat, wound healing

Up-regulation of PSAT1 in colorectal cancer patients regulates by a novel ceRNA network: an integrated systems biology approach (Research Paper)

Maryam Shakarami,[1] Mohammad Rezaei,[2] Mansoureh Azadeh,[3,*]

1. Zist Fanavari Novin Biotechnology Institute
2. Zist Fanavari Novin Biotechnology Institute
3. Zist Fanavari Novin Biotechnology Institute

Introduction: Colorectal cancer (CRC), ranking second most commonly diagnosed cancer and the third most common cancer related to death in the world. CRC is divided into 72% colon carcinoma and 28% rectum cancer, though the occurrence of CRC is sometimes related together. it's for the most part considered a genetic disease, which is characterized by a continuous accumulation of genetic changes. In line with recent studies, numerous risk factors can cause CRC, among these, genetic biomarkers are considered to possess a basic impact on the progress of CRC. Therefore, extensively bioinformatics analysis has been utilized in order to determine these biomarkers as targets for the treatment of CRC.

Methods: At the outset, NCBI Gene Expression Omnibus (GEO) was elected to get the desired GSE (GSE9348), and therefore the gene expression profile (Fig 4) was analyzed by R Studio to search out differentially expressed genes in CRC tissue compared to controls (Fig 5), so the PSAT1 was selected for further studies. The pathways which are related to the PSAT1 gene (Fig 8 – Fig 10) were selected from Reactome pathway database. Then, to pick out various target PSAT1's miRNAs, the Free Online prediction software miRWalk 3.0 was utilized, and the experimental and predictive DIANA LncBase V.2 modules were used to identify the LncRNA list that targeted by miRNAs. Ultimately, the analysis of the pathways concerned in CRC were determined the ceRNAs as one of the post-transcription regulators.

Results: According to GEO analysis of GSE9348 were indicated 13658 up and down regulated genes(Fig 6). Among all these genes PSAT1 was considered as a Up-regulated gene that related to CRC and also serine, threonine, cysteine, methionine, vitamin B6 and carbon metabolism, and biosynthesis of amino acids and cofactors pathways (revealed by KEGG). And miRNAs related to PSAT1 were determined by using the Free Online prediction software miRWalk 3.0 Including hsa-miR-548l, hsa-miR-559, hsa-miR-892a, hsa-miR-5195-3p, hsa-miR-302c-5p. lncRNAs sponge attach to their miRNAs targets and were able to change their expression level therefore these lncRNAs were differentiated with the experimental and predictive DIANA LncBase V.2 modules (PWAR6, SMC2-AS1, SPATA41, TMEM191A, SRP14-AS).

Conclusion: As a result of this study, concluded that PWAR6, SMC2-AS1, SPATA41, TMEM191A, and SRP14-AS lncRNAs act as a tumor suppressor in CRC by inhibiting the function of the hsa-miR-548l, hsa-miR-559, hsa-miR-892a, hsa-miR-5195-3p, hsa-miR-302c-5p miRNAs, so it blocks miRNAs sponging and eventually represses the PSAT1 gene which is an important gene for metabolism and biosynthesis. Therefore, this result may be considered as a potential therapeutic purpose for CRC patients .

Keywords: Bioinformatics, Microarray Analysis, Biomarker, Colorectal Cancer, PSAT1

Use of gene therapy in the treatment of deafness (Review)

Ali Khanifar,[1,*] Rezvan Cheraghale,[2]

1. Kurdistan university of medical sciences
2. Islamic azad university Dezful

Introduction: The process of hearing involves a series of events. The energy of sound is captured by the outer ear and further transferred through the external auditory canal to the middle ear. In the middle ear, sound waves are converted into movements of the tympanic membrane and the ossicles, thereby amplifying the pressure so that it is sufficient to cause movement of the cochlear fluid. The traveling wave within the cochlea leads to depolarization of the inner ear hair cells that, in turn, release the neurotransmitter glutamate. Thereby, the spiral ganglion neurons are activated to transfer the signals via the auditory pathway to the primary auditory cortex. This complex combination of mechanosensory and physiological mechanisms involves many distinct types of cells, the function of which are impacted by numerous proteins, including those involved in ion channel activity, signal transduction and transcription.Deafness or hearing loss in many cases is inherited in families and in some cases the gene causing the disease is known and the ability to predict, prevent or prevent new cases in the family with genetic tests is provided.Genetic deafness is divided into two main types, syndromic and non-syndromic. In the first type (syndromic), in addition to deafness or hearing loss, there are other symptoms and disorders. In the second or non-syndromic case, deafness or hearing loss is the only sign of the disease and is not accompanied by other complications and symptoms. Of course, it should be noted that the inability to speak (dumbness) is the result of deafness and is seen in both groups of patients and the cause is the lack of learning speech skills through listening. The earlier deafness is diagnosed and treated, the less likely it is to be able to speak.Most cases of non-syndromic deafness are permanent and result from damage to the inner ear. The inner ear consists of three parts: the cochlea, the auditory nerves, and the semicircles of balance. Deafness associated with the inner ear is also called sensory nerve.Deafness can also be caused by middle ear disorders, in which case it is called conductive deafness. The middle ear is the location of the hase bones, which are very delicate and thin, which are responsible for transmitting sound.Some deficiencies such as the DFN3 form are associated with disorders in both mid-middle and interior ears. This is a case of a mixed hearing impairment. The deaf and deficit of the hearing is complicated and so many genes have been reported by the researchers.Some of these genes and their performance in deafness are not completely clear. Some genes only create a deaf of denial and some other types. Some of these genes create a syndrome or non-syndromeic type. The genetic deafness in some families is still uncertain, and genetic science has

not yet been able to identify all deafness factors.GJB2 gene mutations are a common factor in non-syndrometic prediction derivations. This gene produces protein-like protein 26. The next gene called GJB6 also produces the protein-protein 30th gene and gene mutations in both of these genes cause deafness.Another type of deafness, DNF3, is caused by the mutation in the POU3F4 gene-dependent gene, and it can not be a good movement of one middle ear bones.The mutations of mitochondrial genes (cell metabolism organs), such as the MT-RNR1 and MT-TS1 gene, have been reported in deaf and low hearing patients. Especially with mutations in the MT-RNR1 gene exposed to deafness due to the use of some antibiotics.

Methods: Gene therapy is a medical field which focuses on the genetic modification of cells to produce a therapeutic effect or the treatment of disease by repairing or reconstructing defective genetic material.The first attempt at modifying human DNA was performed in 1980 by Martin Cline, but the first successful nuclear gene transfer in humans, approved by the National Institutes of Health, was performed in May 1989.The first therapeutic use of gene transfer as well as the first direct insertion of human DNA into the nuclear genome was performed by French Anderson in a trial starting in September 1990. It is thought to be able to cure many genetic disorders or treat them over time.The concept of gene therapy is to fix a genetic problem at its source. If, for instance, in an (usually recessively) inherited disease a mutation in a certain gene results in the production of a dysfunctional protein, gene therapy could be used to deliver a copy of this gene that does not contain the deleterious mutation, and thereby produces a functional protein. This strategy is referred to as gene replacement therapy. The delivery of DNA into cells can be accomplished by multiple methods. The two major classes are recombinant viruses (sometimes called biological nanoparticles or viral vectors) and naked DNA or DNA complexes (non-viral methods). Viruses : In order to replicate, viruses introduce their genetic material into the host cell, tricking the host's cellular machinery into using it as blueprints for viral proteins. Retroviruses go a stage further by having their genetic material copied into the genome of the host cell. Scientists exploit this by substituting a virus's genetic material with therapeutic DNA. (The term 'DNA' may be an oversimplification, as some viruses contain RNA, and gene therapy could take this form as well.) A number of viruses have been used for human gene therapy, including retroviruses, adenoviruses, herpes simplex, vaccinia, and adeno-associated virus. Like the genetic material (DNA or RNA) in viruses, therapeutic DNA can be designed to simply serve as a temporary blueprint that is degraded naturally or (at least theoretically) to enter the host's genome, becoming a permanent part of the host's DNA in infected cells. Non-viral methods present certain advantages over viral methods, such as large scale production and low host immunogenicity. However, non-viral methods initially produced lower levels of transfection and gene expression, and thus lower therapeutic efficacy. Newer technologies offer promise of solving these

problems, with the advent of increased cell-specific targeting and subcellular trafficking control. Non-viral : Methods for non-viral gene therapy include the injection of naked DNA, electroporation, the gene gun, sonoporation, magnetofection, the use of oligonucleotides, lipoplexes, dendrimers, and inorganic nanoparticles. Vector options to introduce gene therapeutics into the inner ear Generally, different concepts are available for gene therapy of hereditary hearing loss. To substitute for the function of a defective gene, an intact copy can be introduced into the relevant cells of the inner ear. Gene suppression, for example through expression of an shRNA that targets the transcript of the mutated gene to prevent its translation, can serve to eliminate dominant-negative effects that may interfere with proper cellular function even if an intact gene copy is provided. Finally, gene correction utilizing gene editing based on designer nuclease systems allows the specific removal of PV, thereby also keeping the natural regulation of gene expression via the physiologic promoter and chromatin environment.Common to all different gene therapy strategies is the requirement for efficient transfer technologies to equip the target cells with expression units for the intact gene or miRNA, for shRNAs, or for the gene editing components. The complex 3D architecture and defined arrangement of the specific cell types inside the cochlea (see Figure 1) excludes ex-vivo cell manipulation and restricts treatment options to in vivo delivery systems. This is in contrast to other organ systems, such as the hematopoietic system, where stem cells can be extracted and re-infused into the patient upon ex-vivo gene therapy. Viruses have evolutionarily co-evolved with their hosts and, as such, have developed specialized mechanisms to enter their target species and cell type(s). Therefore, viral vectors appear to be ideal vehicles to deliver genetic information to the cochlea. Furthermore, the different compartments in the cochlea are filled with lymph, which allows for the distribution of injected viral vectors throughout the cochlea via this intracochlear fluid, while spread to other organs is theoretically limited to the enclosed organ system of the inner ear.Several parameters are important for the success of viral vector-based gene therapy approaches in the cochlea: (1) The vector volume that can be administered is limited. The outer wall of the inner ear is rigid, so that injection of too high vector volumes would increase the pressure and cause hydraulic trauma. Standard injection volumes are 1 µL in mice and are estimated to be 10–30 µL in humans. Thus, high-titer vector preparations are required to allow delivery in a small volume. One advantage for gene therapy application to the inner ear is that the total number of cells present in the cochlea is low as compared to other gene therapy-relevant organ systems, so that a comparably low number of vector particles should suffice to achieve clinical benefit. (2) The endocochlear potential as a result of the different ion compositions of perilymph and endolymph is an important prerequisite for proper functioning of the hearing cascade. Thus, the buffer used to deliver vector preparations should be compatible with inner ear fluids and cell types. (3) Optimal delivery routes to administer viral vectors to the cochlea need to

be investigated (Figure 3), and vector distribution and dissemination from the site of injection need to be characterized. (4) Pre-existing immunity to vector components, such as the capsid, or to transferred genes might limit gene transfer and/or expression efficiency, or cause local inflammation.Currently, three main viral vector systems have emerged for inner ear gene therapy: (1) lentiviral (LV) vectors, (2) adenoviral vectors (AdV), and (3) adeno-associated virus (AAV) vectors. Each of these were tested in in vitro transduction experiments using cell lines, dissociated primary tissue and cochlear explants and were also characterized in vivo in rodent models. Due to space limitations, we will primarily focus on LV and AAV vectors.In contrast to AdV and AAV vector platforms, LV vectors stably anchor their genomic information into the host cell's genome. While this feature is of great advantage when targeting dividing cells – guaranteeing stable, long-term gene addition and transmission to daughter cells – non-integrating vectors have a superior safety profile. Many of the specialized and treatment relevant otic cell types, such as hair cells (HC) and spiral ganglion neurons (SGN), are post-mitotic and thus compatible with non-integrating vector systems. Nevertheless, although naturally integration-competent, LV vectors can be rendered integration-deficient, e. g. upon catalytic inactivation of the viral integrase enzyme, creating so-called non-integrating LV vectors. Although so far only the integrating LV vectors have been tested in the context of otic gene therapy settings.

Results: After identifying the defective gene that led to the deafness, using a suitable vector that carries the healthy gene, injects it into the defective cells to correct the defective gene.Gene therapy can involve not only the insertion of a transgene through efficient viral transduction, but also silencing of a dominant negative allele through miRNA or siRNAs. Off-target effects will be minimized through enhancing the specificity of therapy. Next-generation CRISPR-Cas systems will be harnessed for precise disruption and editing of DNA or RNA for each patient.

Conclusion: Gene therapy is an emerging therapy in the treatment of genetic diseases. This article describes how deafness can be partially controlled using gene therapy. Of course, this requires time to use the right vector to transfer a healthy gene instead of a defective one.Hearing loss is an attractive model for gene therapy approaches as multiple causative monogenetic defects have been identified.The inner ear can be locally targeted with established surgical approaches.Gene replacement and gene correction, e. g. gene editing strategies, can be used to treat hearing loss due to recessive and dominant gene variants.

Keywords: Deafness-Gene therapy-Vector

USING CURCUMIN TO PREVENT STRUCTURAL AND BEHAVIORAL CHANGES OF MEDIAL PREFRONTAL CORTEX INDUCED BY SLEEP DEPRIVATION IN RATS (Research Paper)

Fatemeh Karimi,[1,*] Ali Noorafshan,[2] Saied Karbalay-Doust,[3] Ali Mohammad Kamali,[4]

1. Histomorphometry and Stereology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
2. Histomorphometry and Stereology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
3. Histomorphometry and Stereology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
4. Department of Neuroscience, School of Advanced Medical Sciences and Technologies, Shiraz University of Medical Sciences, Shiraz, Iran

Introduction: Sleep Deprivation (SD) is known to result in a range of neurological consequences in chronically-afflicted subjects. Curcumin, a natural substance, has neuroprotective properties. This study aimed to evaluate the effects of curcumin on the medial Prefrontal Cortex (mPFC) of SD rats

Methods: Male rats were arbitrarily assigned to nine groups, including control, curcumin (100 mg/kg/day), olive oil, SD, SD+curcumin, SD+olive oil, grid, grid+curcumin, and grid+ol ive oil groups. SD was induced by a multiplatform box containing water. After a period of 21 days, the learning and memory of the rats were tested in an eight-arm radial maze. Afterwards, their brains were evaluated using stereological methods

Results: Concomitant treatment of curcumin during SD caused fewer errors during evaluation of the working and reference memory errors in the acquisition and retention phases. The overall volume of the mPFC, Infralimbic Cortex (ILC), Prelimbic Cortex (PLC), Anterior Cingulate Cortex (ACC) and the total number of neurons and glial cells reduced by 20 %-40 % on average in the SD animals in comparison to the control group. This indicated atrophic changes and cell loss in these areas ($p < 0.01$). The dendrites' length and the number of spines per dendrite also reduced by 35 %-55 % in the SD rats compared to the ones in the control group ($p < 0.01$). Yet, treatment of the SD animals with curcumin prevented the atrophic changes of the mPFC, cell loss, and den dritic changes ($p < 0.05$)

Conclusion: SD induced structural changes in the mPFC and memory impairment in the rats. However, curcumin could protect their PFC

Keywords: Sleep deprivation, mPFC, curcumin, stereology, rat

Using natural compounds in novel Nano delivery systems in breast cancer therapy (Review)

Hanieh Ataollahi,[1,*] Helia Ramezani,[2]

1. Faculty of Biological Science, Department of Biotechnology, Islamic Azad University, North Tehran Branch, Tehran, Iran.
2. Faculty of Biological Science, Department of Biotechnology, Islamic Azad University, North Tehran Branch, Tehran, Iran.

Introduction: Introduction: Breast cancer is one of the most common cancers that threaten women's health around the world. Surgery, chemotherapy, irradiation, and hormonal therapy are the four types of treatment options for this disease. Low aqueous solubility, irritant nature, lack of stability, fast metabolism, and nonselective drug distribution are all characteristics of several contemporary anticancer medicines. These characteristics can result in suboptimal therapeutic activity, dose-limiting side effects, and poor patient quality of life. Natural materials have many unique features, including chemical diversity, biological and chemical properties of macromolecular specificity, and low toxicity. As a result, they are good candidates for novel drugs. The aim of this research is to clarify the opportunities and challenges of using natural compounds in drug delivery systems from natural sources in breast cancer therapy.

Methods: Methods: The purpose of this review was to assess new breast cancer therapies that have been reviewed in articles published between 2011 and 2021 using the keywords “breast cancer”, “various drug delivery systems”,and “natural compounds”. These articles were selected and used based on the titles and abstracts of related articles from various databases such as “ScienceDirect”, “Springer”, and “PubMed”. The results were obtained by studying the full text of the selected articles.

Results: Results: Among different drug delivery systems in cancer therapy nanoparticles has a potential impact on various cancer. Improved bioavailability by the aqueous solubility, increased resistance time in the body, and drug targeting to particular tissues in the body are all advantages of nanoparticles. Natural materials are derived from the endogenous chemical compositions of plant extracts, including flavonoids, alkaloids, essential oils, polysaccharides, quinonoids, terpenoids, saponins, and coumarins. According to studies, some natural compounds effective in the treatment of breast cancer include curcumin derived from Curcuma longa, Xanthoumol in hops (Humulus lupulus L.), Garcinol drived from Garcinia indica, Mangiferin, and Luteolin. Due to the positive effects of these natural compounds, they will play a unique role in the development of drug delivery systems.

Conclusion: Conclusion: Using natural compounds in developing new drug delivery systems can be absolutely beneficial and they might have a lot of functional roles instead of synthetic material with a variety of side effects. These natural compounds which are biodegradable and biocompatible would have a certain place in the future owing to their capability to prevent different sorts of cancers.

Keywords: Keywords: Drug delivery, Breast cancer, Natural compounds, Nanoparticles

Using of CRISPR (clustered regularly interspaced short palindromic repeats)-Cas system against Coronavirus disease 2019 (COVID-19) (Review)

Minoo Momenzadeh,[1] Mohammad Amin Talebpour,[2,*] Fatemeh Shamee,[3]

1. School of Medicine, Mashhad Islamic Azad University, Mashhad, Iran
2. School of Medicine, Mashhad Islamic Azad University, Mashhad, Iran
3. School of Medicine, Mashhad Islamic Azad University, Mashhad, Iran

Introduction: Coronavirus disease 2019 (COVID-19) first time broke out in Wuhan, China, and quickly grew into a global pandemic. The virus causing COVID-19 resembles severe acute respiratory syndrome coronavirus (SARS-CoV), therefore, it was termed SARS-CoV-2 by the International Committee on Taxonomy of Viruses (ICTV). The use of CRISPR (clustered regularly interspaced short palindromic repeats)-Cas technology has been identified as a part of adaptive immune system in archaea and bacteria against the virus infections and its applications in humans were found later. Therefore the aim of this study is to investigate the potential use and challenges of CRISPR-Cas-based approaches for possible treatment to combat COVID-19.

Methods: This review was performed within articles published at PubMed, Google scholar and Embase from 2019 to 2021. The keywords were CRISPR / Cas system , COVID-19 and Therapy. By searching this database,79 articles were found, 23 of them were not related with investigating and 15 of them by reading abstract were removed. All articles chosen from English articles.

Results: Finally 41 articles were included in the study. Some studies said that The development of therapeutic drugs against RNA viruses is a great challenge as favourable mutations keep on accumulating in their genome, leading to the development of antiviral resistance. the therapeutic effect of antiviral drugs has not achieved the expected effect, and symptomatic treatment is still the main treatment at present. In some studies, new antiviral therapy has been developed using CRISPR-Cas technology to treat HIV patients and has been said to be safe because it does not cause any side effects for the next 19 months. A Cas 13 strategy based on the corona virus has been developed that can be used as a treatment, although according to some studies, it may face significant challenges in human clinical trials.

Conclusion: The CRISPR / Cas system is a promising tool for the development of therapeutics to eliminate viral infections, although to date no CRISPR-based therapy has been approved for human use. Further studies are suggested to evaluate the potential risks associated with using CRISPR for clinical antiviral therapy.

Keywords: CRISPR / Cas system , COVID-19 , Therapy

UV Photo protecting Capacity of MAAS from Laurencia popillosa – Persian Gulf (Research Paper)

Rezvan Mousavi Nadushan,[1,*]

1. Department of Marine Science, Faculty of Natural Resources and Environment, Tehran North Branch, Islamic Azad University Tehran, Iran.

Introduction: Over recent decades, many people apply chemical sunscreens generally based on physical sun blocks including titanium–dioxide (TiO2) or zinc-oxide (ZnO2), to protect their skin against erythema, sunburn and pigmentation, as well as longstanding consequences, such as photoaging reactions, carcinomas and dermal elastosis. But regular consumption of chemical sunscreens like Avobenzone, Oxybenzone and many others can be absorbed, degraded also may be carcinogenic, photoallergic, neurotoxic or leading endocrine disruption, enhancing pesticide absorption in the body, toxic effects on aquatic organisms and slipping in blood/urine/breast milk. So MAAs are promising substitute for viable chemical sun blockers. Mycosporine-like amino acids (MAAs), are a group of secondary photo stable metabolites existing in many marine algae and soft bodied sessile organisms including red seaweeds. The composition of MAAs show a discrepancy, depending on the species and several environmental factors, especially the intensity and duration of ultraviolet exposure.

Methods: Fresh alienated green/red parts of Laurencia popillosa from Persian Gulf, were frozen by liquid nitrogen, grinded and soaked in methanol at 4 °C for 2 hours. MAAs crude extracts were centrifuged and the supernatant were evaporated, re-dissolved in ultra-pure water. The filtrated MAAs were isolated by reversed-phase HPLC equipped with C18 column. For Evaluation of the Sun Protection Factor (SPF), five different concentrations of crude extract were prepared. Crude extracts were lightly dispersed on the surface of plates containing polymethyl methacrylate (PMMA). Plates were exposed to a radiometer equipped with Hg (Xe) lamp, receiving irradiance of 290 to 400 nm. Finally spectral transmission measured previous to and after UV exposure.

Results: Based on the reference HPLC chromatograms, MAAs were identified in green parts as Shinorine, and in red parts as Porphyra-334, Palythine and Palythinol. The Sun Protection Factor (SPF) for MAAs of mixed extract (green/red parts) were related to extract concentration, reached to 8.69 ±1.06 at 123 mg wet algae per cm-2 which is equivalent to the value of 9.54 ± 1.53 for sunscreen formulation of Avobenzone as a reference.

Conclusion: In summary, this red seaweed is an edible nontoxic algae and it presented a promising photoprotection capacity due to the presence of unique MAAs composition.

Keywords: natural sunscreens, MAAs, Laurencia popillosa, Persian Gulf.

Virulence factors of Aspergillus spp. obtained from Hospital (Research Paper)

Dr.Faezeh Mohammadi,[1,*] Nima Hemmat,[2]

1. Department of Medical Parasitology and Mycology School of Medicine Qazvin University of Medical Sciences
2. Cellular and Molecular Research Center, Research Institute for prevention of Non-Communicable Disease, Qazvin University of Medical Sciences

Introduction: One of the causes of nosocomial infections is the dispersion of Aspergillus spores in the environment. The secretion of hydrolytic enzymes is considered as a virulence factor in Aspergillus species. The aim of this study was to identify environmental Aspergillus isolates via sequencing the beta-tubulin gene and evaluating the ability to produce phospholipase and proteinase in vitro.

Methods: 93 Aspergillus colonies were collected from the emergency, surgical wards, intensive care unit, and operation theatres of two teaching hospitals in Qazvin Province, Iran. The β-tubulin gene region was amplified using polymerase chain reaction (PCR) method, and 40 isolates were sequenced. Evaluation of proteinase and phospholipase production was performed using yeast carbon base (YCB) with bovine serum albumin and egg yolk agar medium, respectively.

Results: Based on β-tubulin sequence, Aspergillus (A.) flavus (30%), A. tuberculosis (25%), A. fumigatus (20%), A. niger (10%), A. sydowii (7.5%), A. terreus (5%), and A. nidulans (2.5%) were identified. Evaluation of extracellular enzymes showed that 82.5% of the isolates had proteinase ability with a mean proteinase of 0.73 ± 0.13, and 52.5% of the studied Aspergillus isolates had phospholipase activity with a mean of 0.81 ± 0.17.

Conclusion: Our study showed that environmental strains have high proteinase production. Therefore, it seems necessary to better understand the association of virulence factors with aspergillosis infection in future studies.

Keywords: Aspergillus; Tubulin; Peptide hydrolases; Phospholipase

Vitamin D receptor(VDR) expression as a prognosis and differential factor in acute myeloid leukemia(AML) (Review)

saman saeidi,[1,*] reyhane shaddel,[2]

1. golestan university of medical sciences(goums)
2. golestan university of medical sciences(goums)

Introduction: Acute myeloid leukemia(AML) is one of the most common kind of leukemia with weak prognosis. vitamin D is effective in immune system and cell division and together with its receptor(VDR),play an important role in many signaling pathways which cause cancer progression. VDR gene is polymorphic (SNP family) Its forms have been studied in relation to the risk of disease in several cancers.in leukemia, Taq I has the most relation with AML among 4 known important polymorphisms.in this review, our goal is to demonstrate beneficial role of VDR in prognosis of AML and its subtypes.

Methods: documentations in this review article are gathered by searching key words such as “Acute Myeloid Leukemia” “VDR” “Prognostic factors” in date bases like PUBMED,GOOGLE SCHOLAR and SCOPUS. At last we chosen 7 article with most related data among 11 that published in last 5 years.

Results: by very important signaling pathways such as MAPK and P13K, VDR play spectacular role in Cell differentiation and by suppressing cancer cells and promoting the proliferation and differentiation of malignant cells, it play role as a Anti-leukemic factor. Given that more immature phenotypes lead to more dangerous prognosis and outcomes, In the field of blood disorders and various subfields of AML, it was observed that VDR null(-/-) mouses develop to have disorders in The process of maturation of myeloid cells. On the other hand, AML subtypes with monocyte differentiation (AML4, AML5) have higher VDR expression compared to immature subtypes. In general, VDR expression seems to be lower in people with AML than in healthy individuals.

Conclusion: in the end, it appears that VDR as a new genetic modulator with its significant role in cell maturation and differential and its Anti-leukemic nature, can play role as a prognosis and differential factor in Acute Myeloid Leukemia. in future, vitamin D and its analogs (specially VDR) can be used in cancer treatment which need more research and information.

Keywords: Acute Myeloid Leukemia - VDR

Vitamin E against Breast Cancer: A review of the preventive and therapeutic role of a Fat-Soluble Vitamin on Breast Cancer (Review)

Mina AkbariRad,[1] AmirAli Moodi Ghalibaf,[2,*] Mina RadMard,[3] Nazanin Forghani,[4]

1. Assistant Professor of Internal Medicine, Department of Internal Medicine, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
2. Student Research Committee, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
3. Student Research Committee, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
4. Student Research Committee, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

Introduction: Today, breast cancer (BC) becomes one of the highest rates of incidence and prevalent malignancies among women in developed and developing countries which causes millions of deaths every year. Unfortunately, too many exogenous and endogenous factors can increase the risk of BC incidence. In this term, some studies and evidence have been indicated that the human immune system and metabolic status as strong potential factors in BC development. On the other hand, vitamins, especially fat-soluble vitamins, are known as critical minerals in metabolic and immune regulation. Therefore, some hypotheses stated the possible preventive and therapeutic role of fat-soluble vitamins including vitamin A, D, E, and K, in BC. So, the current review study is designed to investigate preventive and therapeutic interventions based on vitamin E, as a fat-soluble vitamin, in BC.

Methods: A comprehensive search was done through electronic databases including PubMed, Scopus, Embase, and Web of Science with the keywords “Breast Cancer”, “Vitamin E” and other related MeSH terms up to July 2021. Original studies, review studies, and the references of the review studies were included. Finally, the related studies which investigated the possible relationship between BC and fat-soluble vitamins were reviewed.

Results: Obviously, vitamin E or tocopherol is known as an antioxidant supplement that can potentially protect cells from free radicals DNA, proteins, and cell membrane harming effects. In detail, the protective effects of tocopherol on the DNA and cell lines are due to the decrease in lipid peroxidation by-products. Moreover, several studies indicated the role of vitamin E on activation/inactivation of critical tumorigenic pathways, cell proliferation, energy metabolism, responses to the chemotherapies, and inhibition of the invasion whether metastasis of the malignant cells. Over the molecular and cellular studies, some epidemiological studies demonstrated the protective effects of vitamin E on BC. While some studies indicated the

preventive effects of vitamin E on BC incidence, several studies did not mention any significant relationship between BC prevention and vitamin E status in the body. Also, there was not found a study that indicated any vise verse effect of vitamin E on breast cell lines. There are shreds of evidence that show the therapeutic effects of vitamin E in combination with chemotherapy on BC patients, but the dose/response of this effect is ambiguous.

Conclusion: According to what was reviewed, vitamin E potentially has anti-tumor effects on breast cancer but further studies are needed to determine its sufficient dose and status in the body in this term.

Keywords: Breast Cancer, Vitamin E, Tocopherol, Anti-tumor Agents

Vulvovaginal candidiasis and Nigella sativa L.: A Review Article (Review)

Masoumeh Norouzi Allaleh Korabi,[1,*] Malihe Tabarrai,[2]

1. School of Nursing and Midwifery, Tehran University of Medical Sciences, Tehran, Iran
2. Department of Persian Medicine, School of Persian Medicine, Tehran University of Medical Sciences, Tehran, Iran

Introduction: Vulvovaginal candidiasis (VVC) is one of the most common vaginitis in women of childbearing age. Despite the availability of topical chemical medicine, many women tend to use herbal remedies. The purpose of the current study was to conduct a review on the effect of Nigella sativa in the treatment of VVC.

Methods: In the current narrative review article, the international scientific resources, including PubMed, Web of Science, Scopus, and Google Scholar were searched from inception until March 2021, using keywords such as Vaginitis, Nigella sativa, Black seed, Black cumin, Thymoquinone, Vulvovaginal, candid, vaginitis. The articles presented in conferences and theses were excluded.

Results: Various studies have demonstrated that the oil, extracts, and active ingredients of Nigella sativa, particularly thymoquinone, have antimicrobial and anti-inflammatory effects. The results of the present studies showed that the use of Nigella sativa reduces the symptoms and signs of VVC in women. Nigella sativa also has a therapeutic effect by decreasing the growth of the number of fungal organisms and increasing IgM levels.

Conclusion: The use of Nigella sativa L. seems to be an effective treatment for VVC. Nigella sativa can also be used as an adjunct to the main treatment. Due to the lack of reports of serious side effects, the use of Nigella sativa is recommended for the treatment of VVC.

Keywords: Nigella sativa; Black cumin; Thymoquinone; Candidiasis

Waste Recycling, Extraction of Dirty Gold (Review)

Mohammad Reza Salehi Kia,[1,*]

1.

Introduction: One of the issues in the world is lack of energy and shortage of water resources because of global population growth and global warming. Therefore, specialists seek to produce energy with at least pollution and cost, and to save water consumption through different methods because fossil fuel reserves and drinkable water reserves are disappearing quickly. Therefore, attention is increasing to recycle energy from the solid waste to reduce the consumption of these resources and prevent air pollution. According to the EPA, for every tone of paper that we recycle, we can save 17 trees, 380 gallons of oil, three cubic yards of landfill space, 4,000 kilowatts of energy, and 7,000 gallons of water.

Methods: This study is an experimental research. This project examines production of water from waste through two methods including production of water from biogas and production of it from sewage which require their own processes. System 1: In the production of water from household biogas, there are two tanks. In tank one, there are some blades to chop waste manually. In tank two, there are some micro-organisms that decomposes the waste and produces gas. There are different types of waste with high efficiency in this project such as carbohydrates, proteins, and fats and different types of gases produced by micro-organisms such as methane (CH4), carbon dioxide (CO2), and dihydrogen sulfide (H2s). In this project, the methane is burnt. Thus, water vapor and carbon dioxide are produced. Funnel-shaped structure on top of the benzene lamp collects carbon dioxide and water vapor and conducts them to condenser. In the condenser because of the temperature difference, water vapor from carbon dioxide is separated. Carbon dioxide can be used in industry. Water vapor converts into liquid water which can be applied for agricultural uses, and the main reason in this project is to use it as the drinkable water that needs a lot of experiments. System 2: The production of water from sewage is applicable for the refineries since it produces more gas volume than anaerobic fermentation (biogas). Light hydrocarbons are burnt in refineries and a lot of carbon dioxide and water vapor are produced. Funnel-shaped structure is placed on the top of torches in refineries to prevent entry of carbon dioxide into the earth atmosphere, increases of greenhouse effect, and global warming. It prevents the loss of water vapor in the same way and converts it into usable water by water distillation system. This is a useful and practical project since huge amount of gas is produced from the sewage of refineries.

Results: In both systems, the volume of all produced gases included 65% methane, 34% carbon dioxide, and 10% other gases. Moreover, from 1863 to 1900 liters of methane in both systems, 2900 to 3000 gram of liquid water was produced. The produced liquid water can be converted into the drinkable water which needs a lot of experiments.

Conclusion: All in all, this device is helpful for water production from waste, improving the environment, preventing entry of carbon dioxide into the atmosphere, and reducing of greenhouse effect. This project reduce the pollution that threatens human's health and environment, and protect natural resources with small changes.

Keywords: solid waste, recycling energy, fuel production, protection of environment, fuel produced by waste

What are Stem cells? (Review)

Tarlan Tarhy,[1,*]

1. school

Introduction: What are Stem Cells? The stem cell is the mother of all cells and has the ability to become all the cells in the body. These cells have the ability to self-renewal and differentiate into different types of cells, including blood, heart, nerve and cartilage cells. They are also effective in regenerating and repairing various tissues of the body following injury and can be transplanted into damaged tissues where most of their cells have been destroyed and replace the damaged cells and repair and repair defects in that tissue. . Due to the unique ability of stem cells, these cells are an interesting topic in biology and medical science today. Research in this area has also increased our knowledge of how an organ grows from a single cell and, more importantly, has helped to understand the mechanism by which healthy cells are replaced by damaged cells.

Methods: Stem cells are divided into three categories based on their characteristics: embryonic stem cells, adult stem cells, and umbilical cord blood stem cells. 1.Embryonic stem cells:It is taken from the inner cell mass of a 14-16 day old fetus and is able to make all the cells and tissues of a complete person. 2.Mature stem cells:Cells that separate from the various tissues of an adult after birth are called cells. Hematopoietic stem cells located in the bone marrow, brain, liver and other tissues are the ones that have the power to differentiate into some tissues. 3.Umbilical cord blood stem cells:Extracted from the umbilical cord, they are like bone marrow hematopoietic stem cells Stem-cell therapy is the use of stem cells to treat or prevent a disease or condition. As of 2016, the only established therapy using stem cells is hematopoietic stem cell transplantation. This usually takes the form of a bone-marrow transplantation, but the cells can also be derived from umbilical cord blood. Research is underway to develop various sources for stem cells as well as to apply stem-cell treatments for neurodegenerative diseases and conditions such as diabetes and heart disease. Stem-cell therapy has become controversial following developments such as the ability of scientists to isolate and culture embryonic stem cells, to create stem cells using somatic cell nuclear transfer and their use of techniques to create induced pluripotent stem cells. This controversy is often related to abortion politics and to human cloning. Additionally, efforts to market treatments based on transplant of stored umbilical cord blood have been controversial.

Results: Stem-cell therapy is the use of stem cells to treat or prevent a disease or condition. As of 2016, the only established therapy using stem cells is hematopoietic stem cell transplantation. This usually takes the form of

a bone-marrow transplantation, but the cells can also be derived from umbilical cord blood. Research is underway to develop various sources for stem cells as well as to apply stem-cell treatments for neurodegenerative diseases and conditions such as diabetes and heart disease. Stem-cell therapy has become controversial following developments such as the ability of scientists to isolate and culture embryonic stem cells, to create stem cells using somatic cell nuclear transfer and their use of techniques to create induced pluripotent stem cells. This controversy is often related to abortion politics and to human cloning. Additionally, efforts to market treatments based on transplant of stored umbilical cord blood have controversial.

Conclusion: For over 30 years, hematopoietic stem cell transplantation (HSCT) has been used to treat people with conditions such as leukaemia and lymphoma; this is the only widely practiced form of stem-cell therapy. During chemotherapy, most growing cells are killed by the cytotoxic agents. These agents, however, cannot discriminate between the leukaemia or neoplastic cells, and the hematopoietic stem cells within the bone marrow. This is the side effect of conventional chemotherapy strategies that the stem-cell transplant attempts to reverse; a donor's healthy bone marrow reintroduces functional stem cells to replace the cells lost in the host's body during treatment. The transplanted cells also generate an immune response that helps to kill off the cancer cells; this process can go too far, however, leading to graft vs host disease, the most serious side effect of this treatment. Another stem-cell therapy, called Prochymal, was conditionally approved in Canada in 2012 for the management of acute graft-vs-host disease in children who are unresponsive to steroids. It is an allogenic stem therapy based on mesenchymal stem cells (MSCs) derived from the bone marrow of adult donors. MSCs are purified from the marrow, cultured and packaged, with up to 10,000 doses derived from a single donor. The doses are stored frozen until needed. The FDA has approved five hematopoietic stem-cell products derived from umbilical-cord blood, for the treatment of blood and immunological diseases. In 2014, the European Medicines Agency recommended approval of limbal stem cells for people with severe limbal stem cell deficiency due to burns in the eye.

Keywords: Stem cell , Embryonic stem cells , Mature stem cells ,Umbilical cord blood stem cells

What is cancer? (Review)

Tarlan Tarhy,[1,*]

1. school

Introduction: The Definition of Cancer: Cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body. Cancer can start almost anywhere in the human body, which is made up of trillions of cells. Normally, human cells grow and multiply (through a process called cell division) to form new cells as the body needs them. When cells grow old or become damaged, they die, and new cells take their place. Sometimes this orderly process breaks down, and abnormal or damaged cells grow and multiply when they shouldn't. These cells may form tumors, which are lumps of tissue. Tumors can be cancerous or not cancerous (benign). Cancerous tumors spread into, or invade, nearby tissues and can travel to distant places in the body to form new tumors (a process called metastasis). Cancerous tumors may also be called malignant tumors. Many cancers form solid tumors, but cancers of the blood, such as leukemias, generally do not. Benign tumors do not spread into, or invade, nearby tissues. When removed, benign tumors usually don't grow back, whereas cancerous tumors sometimes do. Benign tumors can sometimes be quite large, however. Some can cause serious symptoms or be life threatening, such as benign tumors in the brain.

Methods: How Does Cancer Develop? Cancer is a genetic disease—that is, it is caused by changes to genes that control the way our cells function, especially how they grow and divide. Genetic changes that cause cancer can happen because: of errors that occur as cells divide. of damage to DNA caused by harmful substances in the environment, such as the chemicals in tobacco smoke and ultraviolet rays from the sun. (Our Cancer Causes and Prevention section has more information.) they were inherited from our parents. The body normally eliminates cells with damaged DNA before they turn cancerous. But the body's ability to do so goes down as we age. This is part of the reason why there is a higher risk of cancer later in life. Each person's cancer has a unique combination of genetic changes. As the cancer continues to grow, additional changes will occur. Even within the same tumor, different cells may have different genetic changes.

Results: When Cancer Spreads A cancer that has spread from the place where it first formed to another place in the body is called metastatic cancer. The process by which cancer cells spread to other parts of the body is called metastasis. Metastatic cancer has the same name and the same type of cancer cells as the original, or primary, cancer. For example, breast cancer

that forms a metastatic tumor in the lung is metastatic breast cancer, not lung cancer. Under a microscope, metastatic cancer cells generally look the same as cells of the original cancer. Moreover, metastatic cancer cells and cells of the original cancer usually have some molecular features in common, such as the presence of specific chromosome changes. In some cases, treatment may help prolong the lives of people with metastatic cancer. In other cases, the primary goal of treatment for metastatic cancer is to control the growth of the cancer or to relieve symptoms it is causing. Metastatic tumors can cause severe damage to how the body functions, and most people who die of cancer die of metastatic disease.

Conclusion: Cancer prevention is the practice of taking active measures to decrease the incidence of cancer and mortality. The practice of prevention is dependent upon both individual efforts to improve lifestyle and seek preventive screening, and socioeconomic or public policy related to cancer prevention.[3] Globalized cancer prevention is regarded as a critical objective due to its applicability to large populations, reducing long term effects of cancer by promoting proactive health practices and behaviors, and its perceived cost-effectiveness and viability for all socioeconomic classes. The majority of cancer cases are due to the accumulation of environmental pollution being inherited as epigenetic damage and many, but not all, of these environmental factors are controllable lifestyle choices. Greater than a reported 75% of cancer deaths could be prevented by avoiding risk factors including: tobacco, overweight / obesity, an insufficient diet, physical inactivity, alcohol, sexually transmitted infections, and air pollution. Not all environmental causes are controllable, such as naturally occurring background radiation, and other cases of cancer are caused through hereditary genetic disorders. Current gene editing techniques under development may serve as preventive measures in the future. Future preventive screening measures can be additionally improved by minimizing invasiveness and increasing specificity by taking individual biologic make up into account, also known as "population-based personalized cancer screening.

Keywords: Cancer, cancer cells, cancer prevention

Woman's fertility behavior in low and middle-income countries(LIMC) (Review)

hanane hamidi,[1,*]

1. Undergraduate nursing student, Khalkhal university, Iran

Introduction: The fertility rate of women in LIMC countries is higher than in rich countries. Reduction in childbearing is key development goal economic and health prosperity of these countries. The gap in women's fertility, health, and economy must be addressed. This study aims to investigate the reproductive behavior and factors affecting it.

Methods: Global Health databases and PubMed were searched in May 2021 for articles published between 2011 and 2021. twenty of them were selected according to our hypothesis and questions.

Results: Some factors associated with high fertility in women are age, education, financial situation, birth interval, marital status, and marriage age. The desire for fertility in poor countries especially in past years was high because they lost their children due to disease. One of the articles states that climate is effective in fertility and populations. unintentional pregnancy occurs as a result of inadequate use of contraception, inadequate knowledge of the fertility period, gender inequality, and lack of women's right to decide. One of the reasons for continuing unwanted pregnancy is the risk of unsafe abortion and Its crime in Islamic countries.

Conclusion: Decreased fertility reduces poverty. Because of early marriage in LIMC, It is necessary to culture building of family planning knowledge in schools which can prevent excessive childbearing and give consulting to increase women's fertility knowledge to limit pregnancies. Access to safe, voluntary services and contraceptives significantly reduces unintended pregnancies and abortions and saves women's lives.

Keywords: fertility, woman's health, and LIMC.

YOGURT AS A VALUABLE PROBIOTIC FOOD FOR HUMAN HEALTH. (Review)

Farzaneh Dianatdar,[1,*] Mohammad Rabbani Khorasgani,[2]

1. University of Isfahan
2. University of Isfahan

Introduction: In the past, people around the world knew that consuming milk and dairy products has a great impact on their health and Even in traditional medicine, some fermented milk products were used. But in the past, the presence of microorganisms in dairy products had not been proven until The Russian scientist Maknikov showed for the first time that the bacteria in Bulgarian dairy products caused the increase in life expectancy of the people of this area, known as Lactobacillus bulgaricus. Probiotic bacteria, as live microbial food supplements, promote microbial balance in the gut. Probiotics are marketed as dietary supplements in the form of tablets, capsules, and dried powders. Recent clinical trials have shown beneficial effects of probiotic bacteria such as preventing diarrhea, balancing the intestinal microflora, stimulating the immune system, modulating systemic immune homeostasis, Reducing the side effects of antibiotics, oral hygiene including gum disease, and eliminating bad breath, anti-tumor properties, and correcting lactose intolerance. The researchers also concluded that probiotic bacteria inhibit the growth of pathogens by producing bacteriocins and organic acids.

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Results: Yogurt and dairy products are also produced in countries such as India and Bulgaria. The existence of Lactobacillus and its health benefits were introduced by a Russian biologist, and the first yogurt factory in Spain was established in 1919. Yogurt can also make vitamin B1 in the gut. Yogurt also contains calcium, phosphorus, magnesium and zinc, and its ability to digest fat, lactose, protein and minerals is better than milk. Yogurt is called a health medicine and yogurt is considered an elixir of longevity. Probiotics are microorganisms that, if taken in sufficient amounts and live, can have health effects on the host. Most bacteria used as probiotics today fall into two categories: Lactobacillus and Bifidobacterium. Bifidobacterium lactis contains an extracellular polysaccharide or polysaccharide capsule that may provide resistance to stomach acid and bile salts. Lactobacillus acidophilus plays a significant role in controlling and lowering intestinal pH by producing acids and thus reducing the growth of many pathological bacteria healing rates of yogurt vary depending on the type of bacteria in it. For example, yogurts containing Lactobacillus acidophilus are more effective in terms of healing properties than other yogurts. Probiotics produce lactic acid and short-chain fatty acids, Which lowers the pH of the colon and increases muscle contractions and smoky bowel movements. Some species of lactic acid and bifidobacteria can increase mucus secretion and reduces constipation by converting bile salts attached to free bile salts and absorbing water into the stool. The active bacteria in yogurt and other yogurt-derived dairy products act as a broad-spectrum natural antibiotic in the intestinal tract. During treatment with oral antibiotics, it is often associated with changes in the gastrointestinal microflora. Consumption of yogurt with Lactobacillus acidophilus and Bifidobacterium longum significantly reduces patients' complaints of gastrointestinal complications and yeast disinfection.

Conclusion: Yogurt is a popular fermented dairy product made by lactic acid bacteria including Streptococcus thermophiles and Lactobacillus delbrueckii subsp. During yogurt production, these bacteria produce lactic acid, lower the

pH, and cause the milk protein to coagulate. Due to the presence of lactic acid, a variety of vitamins and minerals, and microbes, it has a high nutritional value. The therapeutic properties of yogurt have always been considered in ancient and modern medicine. Yogurt may be effective in preventing a variety of cancers, especially colon cancer. Yogurt contains the -prostate gland- and a large amount of natural fatty hormone substances in yogurt Which protect the lining of the stomach wall against the effects of destructive factors such as cigarette smoke and alcohol.

Keywords: Yogurt, yogurt compounds and nutritional value, probiotics, yogurt therapeutic value