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اولین همایش ملی و بین المللی

زیست فناوری و توسعه جهانی

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1. A new method for measuring Escherichia coli (Research Paper)

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Introduction: Nanotechnology is a knowledge and technology that has attracted a lot of attention recently. This technology, which is the new approach of all disciplines, has the ability to produce materials, new instruments by manipulating the atomic and molecular levels. Nano science gives a different attitude about the emergence of new phenomena. In this view, a number of simple interactions between the components of the system, a new property in the whole system, different from the properties of its components, is revealed, which has been largely observed in computer simulations. Nano science gives a different attitude about the emergence of new phenomena. In this view, a number of simple interactions between the components of the system, a new property in the whole system, different from the properties of its components, is revealed, which has been largely observed in computer simulations.

Methods: First, 100 ml of iron dissolving two sulfate and 100 ml of three sulfate iron solution should be prepared and after mixing them together into a human, humans and their contents should be placed on heat and then 20 ml ammonia should be poured into the burt and droplets should be added to the solution, and in addition to adding ammonia, the container containing the solution should be arami. After 20 ml of ammonia is added to the solution, smooth the final solution by filter paper and wait 24 hours until the water that comes with the nanoparticles evaporates and the nanoparticles remain powdered on the filter paper. Then, add the fluorescent colored material (Violet crystal) to the water solution and nanoparticle to absorb the nanoparticle surface and then add the anticorbic to absorb the nanoparticle. Then put the solution, which has the above contents, into a box and create two holes in the box and from one of the holes, uv rays are irradiation into the solution placed in the box.

Results: After producing magnetic iron nano particles and adding fluorescent (violet crystal) and anti core to the solution, the solution contains the above contents into the box and by irradiation of ultraviolet radiation into the solution, mercury vapor lamp produces a wave length in

the ultraviolet region. The bacteria binds to its own anticore and by binding to magnetic nano particles and fluorescence materials, it is produced in the light of the glow. In the absence of fluorescence bacteria, there are no light spots in the presence of mercury vapor lamps, but in the presence of bacteria that are adsorption of nano particles containing anti core and pigment, the intensity of fluorescence increases and is seen as light spots.

Conclusion: Due to the pathogenicity of bacteria and the risk of bacterial infections, rapid measurement of bacteria in disasters such as earthquakes, floods, etc. It becomes necessary. However, using this method without special facilities in the shortest time and with the lowest possible costs, it measured even very small amounts of bacteria that are not measured by standard methods.

Keywords: Magnetic nano particles, coli bacille, anticorbic, fluorescence, ultraviolet radiation

A review of new methods of hemoglobin testing (Review)

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Introduction: Measuring hemoglobin levels in medicine and health is very important for diagnosing and preventing diseases like anemia and blood concentration. Rapid methods and portable devices are vital in emergencies and poor areas with inadequate health facilities. Challenges such as accuracy, measurable interval, maintenance conditions and cost of measuring equipment and devices, environmental compatibility, and reproducibility of hemoglobin measurement method have always been raised. Therefore, a study has been performed on hemoglobin measurement methods and measurement methods adopting microfluidic technology. Also, some examples of microfluidic systems used in hemoglobin measurement are described.

Methods: Reagent-based and reagent-free approaches are two general hemoglobin concentration (Hb) measurement methods on microfluidic systems. The reagent-based methods are Drakbin(HiCN), azide methemoglobin, and sodium lauryl sulfate(SLS). They use reagents to turn the hemoglobin into a chemical product with an absorbance maximum at a specific wavelength. Then the Hb is measured by Beer-Lambertâ€™s law. The Drakbin method employs the solution of potassium cyanide (KCN) and potassium ferricyanide (K3Fe(CN)6) to turn hemoglobin and its derivatives into cyanomethemoglobin(HiCN). HiCN is a stable colored product, which in solution has an absorbance maximum at 540 nm and obeys Beer-Lambertâ€™s law. It was implemented on a microfluidic blood cuvette to measure Hb by Kim et al. The microfluidic blood cuvette was filled with blood samples by capillary force, and hemoglobin levels in the blood were determined by measuring the absorbance of a perpendicular beam incidence at the wavelength of 540 nm. The azide methemoglobin method takes a reagent combination of sodium nitrate, sodium azide, and sodium

deoxycholate that turns hemoglobin into azide methemoglobin with an absorbance maximum at 580 nm. Based on the azide methemoglobin method, Yao et al. have developed a portable Hb determinator, utilizing the disposable microcuvette containing reagent, which could be used for performing the quick test of undiluted and unhemolyzed whole blood within 30 seconds. Correspondingly the SLS method uses the SLS reagent to turn hemoglobin into SLS-methemoglobin with an absorbance at 540nm. Grumann et al. have developed a novel concept for optical beam guidance by total internal reflection (TIR) at V-grooves as retroreflectors which are monolithically integrated on a microfluidic â€œlab-on-a-diskâ€ using the SLS method measurement. The optical path length through a measurement chamber and the sensitivity of colorimetric assays are enhanced compared to direct beam incidence. Reagent-free is a patented method that Hemoglobin fractions are measured from absorbance wavelengths between 400 and 800 nm. The DiaSpect System is a newly developed reagent-free technology for measuring Hb in unaltered blood in a special cuvette that serves as the sampling device.

Results: The Drakbin method is the international standard and consists of inexpensive reagents. Still, the reagents are hazardous because of cyanide presence limiting its use outside the laboratory. Microfluidic blood cuvettes were designed and fabricated to measure Hb by Kim et al. they found that 105 um deep microchannels showed linearity 99.2% compared to 94.5% for 35um deep microchannels. Moreover, microchannel depth must be >100 Î¼m to eliminate blood aggregation. The hemoglobin measuring system developed by Yao et al. is based on the azide methemoglobin method to measure the self-developed reagent microcuvette, which can measure Hb of whole blood within 30 seconds, with the accuracy of 0.1g/dl. Grumann et al. introduced a chip-based, non-invasive method for colorimetric assays with a laser diode and detector. The method is based on the total internal reflection (TIR) at monolithically integrated beam-guidance structured in a polymer substrate. Outstanding features are a high degree of linearity (R^2 = 0.993) between the optical signal and the Hb together with reproducibility of CV= 2.9 % and a time-to-result of 100 seconds. The DiaSpect is a reagent-free hemoglobin measurement device that displays the results within 5 seconds as g/dl in a measurement range of 0 to 25.5 g/dL, And accuracy of 0.3 g/dL for 0 to 20 g/dL and 0.7 g/dL for more than 20 g/dL.

Conclusion: Reagent-free methods for shelf life and environmental compatibility are the priority. However, it has an accuracy of 0.3 g/dl, and they use high technology devices. Contrarily, the reagent-based methods are more accurate than 0.1 g/dl, and they need low-cost equipment. The HiCN method contains hazardous materials, and the Azide methemoglobin method consists of explosives. Nevertheless, the SLS method employs eco-friendly materials.

Keywords: microfluidics, hemoglobin measurement

Activation of Wnt Signaling Through co-receptor LRP6 : an structural dynamics characterization (Research Paper)

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Introduction: Wnt/Î²-catenin signaling is a highly evolutionary conserved pathway that emerges as the regulator of early embryonic development, stem cell biology and growth, and adult tissue homeostasis. One of the principal components of Wnt signaling is LRP6, a co-receptor comprised of two independent functional domains of E1E2 and E3E4 that is a promising target in Wnt-related cancers. In the normal cell state, the pathway is tightly regulated through extracellular ligand antagonists such as WIF-1 (Wnt-inhibitory factor 1), Cerberus, and Dickkopf (Dkk) family members. Dkk1 competes to Wnt to bind to LRP6. Considering the significance of the Wnt signal transduction cascade in various aspects of human health and diseases, also the pivotal role of the co-receptor LRP6 in the pathway activation and inhibition, we decided to explore how ligand-binding changes the dynamic behavior of one of this co-receptor functional domain, E3E4.

Methods: Here, using molecular docking and molecular dynamic simulation, we constructed the Wnt-E3E4 complex and observed the structural and dynamic characteristics of E3E4 upon binding to Dkk1, Wnt3a, and in the free state.

Results: Based on our data supported by previous experimental research, compare to the free state, the E3E4 structural dynamic features are massively affected by ligand binding. Although the activator Wnt3a and the inhibitor Dkk1 have overlapping binding sites on E3E4, they induce exclusive patterns of structural flexibility, inter blades hydrogen bond-formation preference, and specific dynamic characteristics in E3E4 compare to the apo-state.

Conclusion: Altogether, this work warrants structural dynamics insights on E3E4 and provides a useful approach in structural-based drug design against LRP6.

Keywords: LRP6, Dkk1, Wnt3a, Molecular dynamics simulation

Anti-dermatophyte effects of lipid nanofibers produced by Yarrowia lipolytica on oily media (Research Paper)

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Introduction: Yarrowia lipolytica is an oleaginous yeast that grows on a variety of hydrophobic substrates and able to accumulate lipids intracellularly to â‰¥40% of its cell dry. Yarrowia lipolytica is recognized as safe by the Food and Drug Administration and is considered for multiple industrial applications. This yeast is separated from natural samples such as dairy products and meat. Due to the process of pleomorphism, it is highly compatible with various types of oily substrates and produces fatty acids, which are both economically viable and have anti-dermatophyte effects. Dermatophytosis is an infection which able to invade and degrade the skin, nails and hair, caused by kreatinophilic fungi called dermatophyte. Clinical symptoms include itching, scaly, inflammation, redness, and deformity of the skin. Dermatophytosis is a predominance in about 20%â€“25% of all total world populations. Dermatophytosis does not respond well to existing drugs and in most cases recurrence of the infection occurs. Due to the low number of antifungal drugs, side effects, recurrence and prolongation of treatment time, the use of natural products such as electrospun nanofibers with fatty acids have strong anti-dermatophyte effects due to the surface to volume ratio.

Methods: Yarrowia lipolytica(ATCC 18942) was cultured in different media and examined for pleomorphism under microscope. After culturing yeast in media containing oily pulp such as olive, sunflower and sesame, fatty acid production was examined by GC mass and FTIR. Based on the results, olive pulp was selected for the next steps. Nanofibers containing polyethylene oxide and fatty acids were spun by electrospinning. SEM and FTIR were performed to determine the morphology of nanofibers. Finally, the effect of nanofiber treatments by broth micro-dilution, pour plate and well diffusion methods was determined on the growth of Microsporum canis, Trichophyton rubrum and Trichophyton mentagrophytes.

Results: After GC mass and FTIR, the fatty acids extracted from olive oil pulp included oleic acid, palmitic acid, linoleic acid and stearic acid, which had the best production of fatty acids among the pulp, so biomass was measured. Microbial fat extraction was performed on it and the amount of fat and dry weight were 4.07 and 7.83 g/L and the yield of microbial fat production was 52.79%, respectively. In the next step, electrospinning solutions, including solutions of polyethylene oxide, oleic acid and fatty acid extracted from olive pulp were prepared. The polymer solution with ratio of 70:30 was the optimized polymer solution. Optimization of device parameters in the electrospinning process, voltage 15 kV, distance 15 cm, flow rate 1 mlâ„h were obtained. The results of FTIR analysis confirmed the placement of fatty acids in PEO polymer and the type of bond interaction. SEM images, showed fibers without nodes and smooth surface and desirable appearance characteristics. MICs of oleic acid/PEO nanofibers for Microsporum canis, Trichophyton rubrum and Trichophyton mentagrophytes were obtained 0.19, 0.31 and 0.09 ml/ml, respectively. MICs of fatty acid/PEO nanofibers for Microsporum canis, Trichophyton rubrum and Trichophyton mentagrophytes were obtained 0.021, 0.021 and 0.044 mg/ml. MFCs of oleic acid/PEO nanofibers for Microsporum canis, Trichophyton rubrum and Trichophyton mentagrophytes were obtained 0.38, 0.62 and 0.18 ml/ml. MFCs of fatty acid/PEO nanofibers for Microsporum canis, Trichophyton rubrum and Trichophyton mentagrophytes were obtained 0.042, 0.042 and 0.088 mg/ml.

Conclusion: Yarrowia lipolytica is a native and available yeast that is capable of producing fatty acids in low-cost, available and unused substrates. The fatty acids produced by this yeast can be used in various fields such as pharmaceutical and food and have strong anti-dermatophyte effects that can be a good alternative to existing anti-dermatophyte drugs. These fatty acids have no side effects and prevent recurrence of the disease and based on the results, having fungicidal effects on dermatophytes. On the other hand, pulp is an unused compound can be used to produce the necessary compounds by native yeasts very cheaply.

Keywords: Yarrowia lipolytica, Electrospining, Yeast, Lipid, Dermatophyte

Antibacterial, antioxidant and anticancer effects of the hydroalcoholic extract of Eucalyptus Globulus leaf growing in the north of Iran (Research Paper)

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Introduction: Eucalyptus Globulus is the kind of Myrtaceae trees that is originally from Australia and forms a dense forest. Its height is from 30 mm to 145 m. and its stem diameter reaches 25 m. This research aims at studying the antimicrobial, antioxidant and anticancer effects of the hydroalcoholic extract of Eucalyptus Globulus leaf.

Methods: First, Eucalyptus Globulus leaves were powdered, and the hydroalcoholic extract was prepared with using ethanol solvent 70%. The antimicrobial effect of this extract was examined on Staphylococcus aureus, Escherichia coli, Listeria monocytogenes, and Salmonella typhimurium bacteria using antibiogram method. In addition, MIC and MBC values of Eucalyptus Globulus hydroalcoholic extract were determined. The antioxidant effect was examined using DPPH method. To test the anticancer effect of the extract, MTT method on gastric cancer cell line (AGS) was used.

Results: The diameter of the inhibition zone of Eucalyptus Globulus hydroalcoholic extract in well method on Escherichia coli, Staphylococcus aureus, Listeria monocytogenes, and Salmonella typhimurium was 12, 22, 28, and 15 mm, respectively, In addition, MIC and MBC in Escherichia coli and Staphylococcus aureus were 0.625 and 1.25 mg/ml, in Listeria monocytogenes was 1.25 and 5 mg/ml, and in Salmonella typhimurium was determined 5 and 10 mg/ml, respectively. The maximum antioxidant activity was recorded in 9 mg/ml extract concentration. Cells viability in MTT test was obtained 79.9% in the presence of extract.

Conclusion: Eucalyptus Globulus extract has antimicrobial, antioxidant and anticancer properties and can be a proper alternative for infection treatment, reducing cancer growth and as an alternative to chemical preservatives in the food industry.

Keywords: Eucalyptus Globulus, Hydroalcoholic extract, antimicrobial, antioxidant, anticancer

Antifungal activity of Rosemary oil extract against and its effect on the Afl.1 gene expression in the Aspergillus flavus by Real Time-PCR (Research Paper)

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Introduction: Investigating about the extract of Rosemary in various groups of fungi and this extractâ€™s minimum effective deterrence density on types of fungi and also the survey of this extract in expressing the Afl.1 gene in Aspergillus flavus is the main target of this research. Rosemary is a very important medicinal herb. Although its antimicrobial effect is fully considered, but its effect on toxin-causing and pathogenic funguses is not studied very much. Therefore, considering the limitation of antifungal drugs, chemical effects, and drug resistance of them, it seems the access of reaching an effective herbal medicine really matters. Since the Aflatoxin is concerned in various food, livestock, pharmaceutical, and medical industries, this research illustrates the mchanism of growth containment by this fungus.

Methods: First of all we cultivate Aspergillus flavus in sabouraud dextrose agar perimeter and then we put Rosemary impregnated paper disks on the surface of perimeter to determine the anti-fungal effect with disk difussion method and creation of inhibition zone then with the help of 10 standard sterile tubes (macrodeloution method) we dilute Rosemary extract in the perimeter of sabouraud dextrose broth to gain this extractâ€™s effective concentration and finally Rosemaryâ€™s effect on expressing the Afl.1 gene was examined by Real Time-PCR.

Results: Achieved results indicate that the extract of Rosemary on various types of fungi has an inhibitory effect. The average diagonal of bright anti growth haloes are about 16-18 mm. Therefore the minimum density of deterrence Rosemary extract or MCI for Asperjillus flavus is 3 to 5 mg per liter and the results of Real Time- PCR confirm this inhibitory effect on expressing the Afl.1 gene which produces Aflatoxin in molecular level.

Conclusion: The extract of Rosemary can have a considerable inhibitory effect on expressing the Afl.1 gene and production of Aspergillus flavus.

Keywords: Asperjillus flavus, Rosemary, Afl.1, RT-PCR

Aptamer-based biosensors for food safety analysis (Review)

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Introduction: Food safety is a key factor for achieving public health. Food contaminants such as mycotoxins, pathogens, antibiotic residues and pesticides are major sources of human exposure. Consequently, development of a sensitive, rapid, user friendly and cost effective analytical methods are needed for food safety monitoring. Biosensors have been introduced as on-site promising tools which overcome limitations of the conventional analytical methods.

Methods: As one of the innovative types of biosensors, aptamer based biosensors are efficient detection platforms for food contaminants. Aptamers as selective recognition elements are single stranded sequence of RNA or DNA, which can selected from SELEX process. Aptamers can bind to targets with high affinity through hydrogen bonding, electrostatic and van der waals interactions. High affinity, chemical stability and easy synthesis are the advantages of aptamers over antibodies. Using aptasensors for determination of veterinary drugs such as antibiotics and hormones have been reported. Aptamers have been recognized as innovative common recognition elements for detection of tetracyclines, Î²-lactames and sulfamethazine in milk, honey and chicken. Also, aptamer based biosensors for selective detection of aflatoxins in food samples have been reported in several studies.

Results: The signal changes which generate from biological reactions can be measured using electrochemical techniques. Depend on these measurable parameters, electrochemical biosensors are divided to voltammetric, amperometric, potentiometric and impedimetric. The important factors which influence on biosensor performance are electrode surface, immobilization method and detection technique. Employing nanomaterial engineering in recent years led to improve the sensitivity of electrodes as transduction elements. Carbon nanomaterials, metal nanomaterials and magnetic nanoparticles are the most applied ones for biosensor fabrication.

Conclusion: Food industry need low cost, rapid and precise detection devices for food analysis. Aptamer based biosensors are promising devices for detection of food contaminants. Selectivity, stability, sensitivity and practicability are the factors that denote the performance of a biosensor. Performance of sensitive biosensors which can detect multiple analytes in multiplex systems are trends in future studies.

Keywords: food saftey, biosensor, aptamer, antibiotic residues, aflatoxins

Bioinformatic analysis of regulatory relation between MALAT1 lncRNA and its related microRNAs in breast cancer and studying MALAT1 lncRNA expression in breast carcinoma tissues (Research Paper)

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Introduction: Breast cancer is known as a heterogeneous disease that has different biological and phenotypic features and these factors have made the diagnosis and treatment of this disease challenging. The role of non-coding RNAs has been proven to be an important factor in growth and development of tumor; up-regulation of many of them has been reported in various types of cancer. Misregulation of non-coding RNAs such as Long non-coding RNA (lncRNA) and microRNAs has been reported in breast cancer. Some types of lncRNA molecules can inhibit the function of microRNA molecules by sponging them, thus they regulated gene expression.Â This study evaluated the expression of MALAT1 LncRNA and related microRNAs in breast cancer after bioinformatics analysis of the regulatory relationship between MALAT1 LncRNA and one of the candidate miRNAs, miR-125b, in breast carcinoma tissue samples.

Methods: Â This study consisted of two parts: bioinformatics and laboratory. In the bioinformatics section, the relationship between MALAT1 LncRNA and related microRNAs in breast cancer was investigated and after data mining, the regulatory relationship between MALAT1 and some miRNAs, including miR-125b, was identified. In the practical part, after RNA extraction, cDNA synthesis, the expression of MALA1 lncRNA and miR-125b in breast tumor tissue samples was compared to the paired adjacent normal samples by real-time PCR.Â Â

Results: Â The results of this study showed the up-regulation of long non-coding RNA in MALAT1 in tumor tissue samples compared to non-tumor samples (*** P <0.001). There was also a significant down-regulation of miR-125b expression levels in breast tumor specimens (*** P <0.001). The inverse expression link between the long non-coding RNA of MALAT1 and its regulated microRNA, miR-125b, indicates a regulatory link between them in breast carcinoma. Also, there was a correlation between the

expression levels of these non-coding RNAs and the clinical and pathological features of the disease, such as disease progression and HER2 activity status. Â

Conclusion: The regulatory relationship between MALAT1 lncRNA and miR-125b with up-regulation of MALAT1 and down-regulation of miR-125b was proved in this study. It seems that these two non-coding RNAs can have biomarker capabilities in the diagnosis of breast cancer. Â

Keywords: Breast carcinoma, Non-coding long RNA, Micro RNA, Diagnostic biomarker

Bioinformatics study of the effect of bacteriocins on SARS-CoV2 (Research Paper)

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Introduction: The world has been facing the Coronavirus pandemic for more than a year and this problem still persists. Many people have died from the disease, and the social and economic conditions of most people around the world have been affected by the virus. Due to many efforts to treat SARS-CoV2, no effective treatment has yet been identified. To reduce the research time and increase their effectiveness, computer tools can be used to investigate the interaction of compounds and drugs with the SARS-CoV2, and finally the compounds that have the most interaction with the virus enter the in vitro phase of research. Accordingly, in the present study, the interaction of bacteriocins with pathogenic proteins of the SARS-CoV2 was investigated in silico. Bacteriocins are small microbial peptides produced by bacteria to overcome other bacterial strains.

Methods: The molecular structure of Microcin and Colicin from Escherichia coli and Marcescin from Serratia marcsecens was obtained from the articles and plotted using ChemDraw software. The structure of SARS-CoV2 pathogenic proteins including 3CLpro, PLpro, RdRp, Spro and Mpro was obtained from the protein databank (PDB). Molecular docking was performed with Mulegro Virtual Docker software and its three-dimensional shape was observed with Mulegro Virtual Viewer.

Results: Among the three bacteriocins studied, Marcescin was able to dock with Mpro and Spro with docking energy of -126.42 kJ/mol and -108.58 kJ/mol, respectively. But the other two bacteriocins did not interact with SARS-CoV2 proteins. Residues involved in the interaction between Marcescin and Mpro were included Gln 110, Thr 111, Gln 127, Ser 158, Thr 292 and Phe 294. Residues involved in the interaction between Marcescin and Spro were included Gln 110, Asn 151, Cys 160 and Phe 294.

Conclusion: Although bacteriocins are antibacterial compounds, in the present study, it was shown that Marcescin can also have antiviral effects. However, after further experiments, especially in vitro tests, a definite report can be made about the anti- SARS-CoV2 effect of this peptide.

Keywords: SARS-CoV2, Bacteriocin, Marcescin, Molecular Docking

Biotechnology and application of monoclonal antibodies in the diagnosis and treatment of diseases (Review)

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Introduction: Monoclonal antibody biotechnology uses immune cells to make a special protein called an antibody. From this property and ability of B lymphocytes It is used to make specific antibodies called monoclonal antibodies because of the specificity of monoclonal antibodies as a powerful tool for detection the amount and position of a substance is used. The aim of biotechnology research is the application of monoclonal antibodies in the diagnosis and treatment of diseases.

Methods: In this review study; Information on the use of monoclonal antibodies in the treatment of diseases from such databases SCOPUS; SID; pubmed and magiran Qualitative data analysis was performed.

Results: Today Monoclonal antibodies are widely used in the diagnosis and identification of a large number of microbial infections. Also, because cancer cells are biochemically different from normal cells, we can make monoclonal antibodies that are specific to Cancer cells attach In addition to detecting human disease from monoclonal antibodies, a molecule with therapeutic potential can be isolated from a mixture of thousands of other molecules.

Conclusion: we hope to use monoclonal antibodies in the treatment of cancer and other diseases. By attaching radioisotope material or a toxin to the anti-cancer monoclonal antibody, we can deliver the deadly substance to the cancer cell directly by shortening normal cells.

Keywords: biotechnology ; antibody ; Monoclonal; Treatment and clinical medicine, diagnosis

CAR-T Cells Immunotherapy, A New Approach for the Treatment of Triple Negative Breast Cancer (Review)

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Introduction: Triple-negative breast cancer (TNBC) is an aggressive disease that lacks targeted therapy. It is estrogen and progesterone receptor negative, lacks human epidermal growth factor 2 (HER2) gene, and is very aggressive. There are currently no treatments for TNBC. Immunotherapy with chimeric antigen receptor (CAR)-T cells is a novel immunotherapy approach and has been effective in treatment of some hematologic tumors. However, its efficacy on solid tumors is under research.

Methods: In this study, we reviewed CAR-T cell-based immunotherapeutic strategies for TNBC. We searched articles from 2016-2021 within Google scholar, PubMed and ScienceDirect with keywords Triple-negative breast cancer and CAR-T. Our exclusion criteria were review articles. Sixty-nine articles were found and sixty-one of them were removed after reading the title or abstract. Eight articles were selected for this review.

Results: Therapy with TEM8-specific, EGFR-specific, AXL, ICAM1-specific, MUC28z and NKG2D CAR-T cells successfully reduced tumor size in both murine and patient-derived TNBC cell lines and induced regression and stasis. These CAR-T cells were chosen based on protein expression within the tumor micro-environment. These CAR-T cells increased pro-inflammatory cytokines like IFN-Î³, TNF-Î± and IL-2, enhanced T cell persistence and displayed potent cytotoxic capacity. However, according to results, CAR-T cells were still less effective in TNBC solid tumors than in hematological malignancies. In ROR1-specific CAR-T cells, therapeutic effects were impaired due to anti-inflammatory cytokines such as TGF-Î² in tumor environment. Combining ROR1-specific CAR-T cells with SD-208, a TGF-Î² blocker reduced the immunosuppressive effect.

Conclusion: These results demonstrate that immunotherapy with CAR-T cells can be a promising approach for TNBC treatment. CAR-T cell therapy is very challenging for solid tumors like TNBC due to the immunosuppressive microenvironment in the tumor site. Combining CAR-

T cell therapy with other therapies or blocking anti-inflammatory cytokines may offer a better approach for CAR-T cell therapy for solid tumors.

Keywords: CAR-T, TNBC,Â Breast Cancer,Â Immunotherapy

Colorimetric nanoprobe-based detection of Helicobacter pylori using direct targeting of nucleic acids (Research Paper)

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Introduction: Helicobacter pylori is known as a type 1 carcinogen and causes gastritis, stomach ulcers, gastric cancer, and mucosa-associated lymphoid tissue (MALT). H. pylori infection is mainly diagnosed by non-invasive methods such as urea breath tests, or by invasive methods such as endoscopy. Due to the importance of rapid diagnosis of H. pylori, we developed a nanoprobe-based method for direct detection of the target in the cells.

Methods: A specific target region was selected, and complementary probes were designed. The probes were used to functionalize gold nanoparticles. The genomic DNA contents of the samples were retrieved by the boiling method. The nucleic acid content of the cells was used for the further detection procedure. After a denaturation and annealing stage, magnesium chloride salt was used for induction in the colorimetric assay.

Results: The results show that the designed Au-nanoprobes were capable of attaching to the target region specifically among ten different bacteria, providing a specific colorimetric detection approach in less than 10 min. Moreover, the optimized concentration of the salt yields an optimum color differentiation between the positive and the negative samples. In positive samples, the nanoparticles stayed dispersed (red) due to a successful hybridization while in negative samples, aggregation occurred due to lack of a complementary sequence resulting in a blue shift.

Conclusion: Non-crosslinking gold nanoprobe method could be used as a simple, rapid, affordable method to nanodiagnosis of H. pylori and help restraining the spread of H. pylori infection.

Keywords: Helicobacter pylori-Gold nanobiosensor-Nanodiagnosis

Comparison of anti-cancer effects of Lentinan and Docetaxel nanofibers on the expression of cancer-inducing genes (Research Paper)

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Introduction: Lentinula edodes, also known as Shiitake, is a native basidiomycete that is both edible and medicinal. This Mushroom plays a considerable role in cancer therapy as an adjuvant and enhancing the quality of life of patients due to its bioactive compounds and polysaccharides with anti-cancer and anti-tumor properties such as Lentinan in China and Japan. Lentinan rigid polysaccharides can participate in the fabrication of various types of nanocomposites. The use of compounds from this medicinal mushroom in cancer treatment will be useful because they will suppress the expression of genes that are effective in causing cancer along with current medicines. HER3 is a member of the epidermal growth factor receptor (EGFR) family, which is overexpressed in 20-30% of invasive breast cancers. This gene forms a heterodimer with other HER family members. Breast cancer is highly prevalent among women all over the world. Therefore, the use of natural and native compounds with high effectiveness without side effects along with commonly used antineoplastic drugs (which have various side effects, are often costly, and out of reach of patients) would have synergistic effects in reducing the invasion of cancer cells.

Methods: First, the optimal conditions for solid and liquid culture media, acidity and temperature for the growth of Lentinula edodes (TMU340) mycelium were determined. Also, by using the lyophilization process, the ratio of wet to dry weight of mycelium and fruiting bodies of this mushroom was determined. Isolation and extraction of Lentinan polysaccharide were performed using 60 Â°C hot water method, deproteinization by Sevage method, extraction, and precipitation with absolute ethanol from mycelium and fruiting body; By using the DEAE Sephadex A-25 ion-exchange chromatography, polysaccharide was purified and the concentration was obtained by phenol-sulfuric acid test. Then electrospinning was used to spin nanofibers, and SEM and FTIR were

used to study the morphology and composition of these nanofibers. MCF-7 cancer cells were treated with different concentrations of treatment groups, including PVA /Lentinan /Docetaxel, PVA/Docetaxel and PVA/Lentinan nanofibers with positive control of Docetaxel, Lentinan, and PVA. MTT Assay was used to calculate the cell viability percentage and expression of the HER3 gene was determined using Real-Time PCR compared to untreated controls.

Results: The optimal liquid and solid culture media were determined as PDA and PDB media, respectively. Also, the optimum temperature and pH for the growth of mycelium of this mushroom was determined as 25 Â°C and pH 5.5 during 14 days of growth. Wet to dry weight ratio in the mycelium and the fruiting body was calculated as a 10:1 ratio. The results of the phenol-sulfuric acid test determined a higher concentration of Lentinan in mycelial extraction than the fruiting body, equal to 0.243 mg/ml. Optimal electrospinning conditions were determined for 1 kV, 15 cm distance, and 1 ml/h flow rate. The cell viability percentage of MCF-7 cells were reported as 28.5 percent for 72 hours after treatment with triple PVA/Lentinan/Docetaxel nanofibers. The expression level of the HER3 gene was 0.52 compared to the control group at the most effective concentration for 72 hours; Also, the expression level of this gene by the treatment of free Lentinan was 0.9 and free Docetaxel was 0.62, which indicates a synergistic effect and suitable for drug supplementation.

Conclusion: Lentinula edodes is an inexpensive, affordable, easy to grow, and native mushroom. The compounds and bioactive polysaccharides of this mushroom have given special medicinal value to it. The reducing effect of polysaccharides of this mushroom on the expression of the HER3 gene can be effective in preventing the progression of cancer by controlling the expression of genes involved in cancer with conventional chemotherapy drugs. Triple PVA/Lentinan/Docetaxel nanofibers have a suitable synergistic effect over time, which has a favorable anti-cancer effect by reducing the expression of the HER3 gene and is a suitable drug delivery system.

Keywords: Lentinan, Electrospinning, Breast cancer, Shittake, Docetaxel

Comparison of the population of Traplus agilis in Sistan with otherÂ populations of this species in some parts of Iran (Research Paper)

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1.

Introduction: The genus Trapelus has 13 species, of which Trapelus agilis is one ofÂ its members, which is distributed in Iran, Afghanistan, Pakistan,Â India and Central Asian countries. Sixteen specimens of T. agilis wereÂ collected from the Sistan Basin and the Central Plateau of Iran. 18Â morphological traits by SPSS software. v16 was analyzed. For molecularÂ studies, the 16SiRNA mitochondrial gene was amplified by a polymeraseÂ chain reaction and sent to Macrogene, South Korea, for sequencing. ToÂ investigate phylogenetic relationships between populations, unmodifiedÂ genetic distance was taken in 6.MIEGA software. Plotype networks wereÂ plotted to study genetic divergence in Popalt software. GenealogicalÂ trees with maximum probability, maximum parsimony and BayesianÂ inference were plotted. Morphological results show the morphologicalÂ diversity among the populations of Sistan. Molecular results alsoÂ indicate that genetic diversity among populations in T. agilis is high.

Methods: After determining the sampling stations in Sistan, includingÂ Miankangi, Posht Ab, Shahraki and Naravi water slopes and Zabol, asÂ well as determining these stations in the range of distribution ofÂ this species in the central plateau of Iran, sampling was done.Â Sampled areas are provided along with the exact address of the sampleÂ collection site. Sampling was done entirely by hand, but this requiresÂ tools and equipment such as suitable gloves, a bag for storing liveÂ specimens, proper storage containers, a geolocation device (GPS), andÂ a camera. The collected samples are transferred to the laboratory. Û²Û²Û¸/ÛµÛ°Û°Û° SPSS 16 software was used for statistical analysis of morphologicalÂ data. Multivariate statistical analysis was used to compareÂ populations. Principal component analysis or PCA is one of the mostÂ popular multivariate analysis methods. DNA extraction is the first step in any molecular method. AfterÂ collecting samples from the environment and transferring them Tissues from the tongue and thigh muscles were prepared in theÂ laboratory and used for molecular studies. DNA extraction wasÂ performed by ammonium acetate salt method, the

steps of which are asÂ follows: Transfer the finely chopped tissues to 2ml tubes. The tube is thenÂ placed in a laboratory temperature for about 2 hours or in anÂ incubator for about 30 minutes at a temperature of about 40 Â° C untilÂ the alcohol in the tissue is completely evaporated. Û². Then inside the tube 700 Î¼l buffer (B) or Lysis buffer + 40 Î¼l SDS Add 20% +10 Î¼l of proteinase K and then combine them thoroughly byÂ vortexing. The tubes are then transferred to an incubator at 55 Â° CÂ for 18-20 hours. Ù£. After 18-20 hours, the lysed samples are taken out of the incubatorÂ and 340 microliters of four molar ammonium are added to each tube. 4. To mix the ingredients thoroughly, gently lower and lower the tubesÂ several times, then turn it to Place at laboratory temperature for 40 to 60 minutes, then centrifugeÂ the tubes for 4 minutes at 4 Â° C at 13,000 rpm. 5. Gently remove the upper liquid content of the precipitated area andÂ transfer to a new 2 ml tube, then add 1000 Î¼l (1 ml) of coldÂ isopropanol (-20) or 100% alcohol to each, then add the tubes toÂ Gently stir several times to mix thoroughly, then centrifuge the tubesÂ for 30 minutes at 4 Â° C at 14,000 rpm. Discard the top 6 DNA sediment liquids and allow the remaining alcoholÂ in the tube to evaporate at laboratory temperature for a period ofÂ time. Once the alcohol is completely dry, add 100 Î¼l of doubleÂ distilled water to each tube, then refrigerate the samples at 4 Â° CÂ for at least 24 hours to dissolve the DNA in water. 7. To evaluate the quantity and quality of the extracted DNA, a tattooÂ therapist was used (Figure 2-3). For this purpose, first the device isÂ calibrated with distilled water, then we put 2 microliters of DNA onÂ the device and its quality and quantity are measured. In addition toÂ the light absorption ratios of 260/260 and 260/230, this device alsoÂ calculates the net concentration of soluble DNA. The calculated ratioÂ must be between 1. 8 to 2. 2. The closer this number is to 2, the higher the qualityÂ of the extracted DNA, and if it is less than 108, it indicates theÂ presence of different proteins in the extracted DNA. On the otherÂ hand, if this number is more than 2, it indicates the presence ofÂ organic matter in the extracted DNA.

Results: Morphological results The analysis of principal components analysis onÂ the morphological traits of I. agilis in Sistan Basin was able toÂ determine the morphological diversity among Sistan samples. The firstÂ component of this analysis includes 69. 81% of the total variance andÂ the second component includes 19. It is 46% of the total variance. Molecular results In order to study and evaluate the taxonomic status of T. agilis, dataÂ from the mitochondrial DNA sequence of gene 165 with a

length of 470Â nucleotides were analyzed for 16 samples. I ruderatus was consideredÂ as an external group. After grouping the populations, the genetic distance between them wasÂ calculated. The results show that the highest genetic distance betweenÂ Kerman cloud is with other clouds and the lowest genetic distance isÂ between Gonabad and Ghaen clouds. Sistan cloud has the highest geneticÂ distance with Mazandaran, Kohgiluyeh and Boyer Ahmad clouds. After drawing the genealogical tree by BI method, the ML genealogyÂ tree and the MP parsimony tree, which is considered as an outgroup inÂ all three trees of Irapelus ruderatus, have a similar pattern andÂ generality in all three trees for species I. agilis is shown asÂ follows: Clouds of Mazandaran, Kohgiluyeh and Boyer Ahmad, Cloud T.Â Sanguinolenfus and a specimen of Sistan are in a tributary, and theÂ clouds of Qaen, Gonabad, and the cloud of Sistan are in a tributary.Â Cloud Sitan is scattered among the branches. Kerman cloud is separatedÂ from other clouds

Conclusion: One of the most controversial groups of the Agamidae family is theÂ Irapelus agilis species collection, which has been the subject of manyÂ reptile journals and magazines since 1804, when Olivier collected itÂ from the outskirts of Baghdad in eastern Iraq. This species speciesÂ has a very wide distribution range within the territory of Iran,Â Pakistan, Afghanistan and Central Asian countries. The populations ofÂ the southern regions (southern Iran, southern Pakistan andÂ Afghanistan) show great diversity in morphological traits, whichÂ indicates a long history of evolution. These populations areÂ traditionally divided into three subspecies, the populations ofÂ eastern Iraq if any, the populations of southwestern Iran and centralÂ Iran as subspecies of T. a. are considered agilis. While theÂ populations of eastern and southeastern Iran, southern Afghanistan,Â southern and western Pakistan and northern India are considered as theÂ second traditional subspecies of Ta, isolepis. In contrast, theÂ populations of the northern part (Northeast of Iran and Central Asia)Â are a homogeneous group of T. a. sanguinolentus, which has low phenotypic changes and indicatesÂ the possibility of their recent invasion of the southern part of theÂ post-Tuscan police icy period. In 1961, Leviton and Anderson demonstrated the statisticalÂ significance of the diversity of scales in different populations.Â Wettstein in 1951 stated that there are three subspecies agilis, isolepis, Sanguinolentus are not acceptable because theseÂ parts are not based on morphology. A collection of 51 samplesÂ collected by Anderson from southwestern Iran

in 1963 has 76-95 scalesÂ around his body. 18 samples by Tuck collected from northeastern Iran in 1979. He has 74-63 scales allÂ over his body. Six examples from Afghanistan show that there are 76-72Â scales. 9 examples from Kandahar in southeastern Afghanistan haveÂ 74-60 scales. The specimens of Kandahar (southeast Afghanistan) areÂ somewhat smaller than the specimens of the lowlands of Afghanistan andÂ Iran. Finally, Rastegar Pouyani in 1999, two subspecies of T. , a,Â pakistanesis and Ta khuzistanesis for species T. introduced agilis. Among theseÂ subspecies, there are three subspecies in Iran These are: T. , a, agilis, T. a. sanguinolentus, T. a. khuzistanesis Is In this study, different populations (T. agilis, Olivier (1804) in theÂ Sistan Basin and some areas of the Central Plateau of Iran wereÂ studied based on morphological and genetic data. The existence ofÂ different ecological conditions in the habitats occupied by this taxonÂ is attributed to the fact that it lives in different habitats and theÂ habitats are at different levels in terms of height. Genetic results show that the clouds of Mazandaran, Kohgiluyeh andÂ Boyer Ahmad, the cloud of T. sanguinolents and a specimen of SistanÂ are in a fork, and the clays of Qaen, Gonabad, and a cloud of SistanÂ are in a fork. Kerman cloud is separated from other clouds. On the other hand, KermanÂ cloud has the greatest genetic distance with other clouds. AccordingÂ to the haplotype network, Ghaen and Gonabad clouds are shared withÂ each other and Mazandaran, Kohgiluyeh and Boyer-Ahmad clouds alsoÂ share their haplotypes, which is probably due to the shortÂ geographical distance or the same living conditions between theseÂ clouds. There are several different haplotypes of Cloud Sistan betweenÂ haplotypes, indicating genetic diversity. Kerman haplotype with highÂ genetic diversity is placed separately and needs comprehensive andÂ extensive studies. On the other hand, the existence of a very largeÂ area of â€‹â€‹the Central Plateau has caused the rapid distribution ofÂ this species on the plateau and the existence of habitat diversity andÂ geographical barriers in a very diverse The Central Plateau of Iran and the Sistan Basin have probably led toÂ the localization of this species and the occurrence of genetic andÂ morphological variations.

Keywords: Genetic distance, phylogeny, morphology

Comparison of the results of biological dressing treatment of xenoderm with traditional treatment method in large burns (Research Paper)

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Introduction: Burns are an important cause of death and disability in the world and today biological dressing is an important part of burn treatment in advanced centers. With this method, the percentage of mortality in comparison with the level of burn from 50% mortality in 30% burn has reached the same amount in 80% burn. Due to the lack of experience in the widespread use of biological dressings in developing countries, the aim of this study was to compare the results of the use of biological dressings with traditional methods in patients with extensive burns.

Methods: In this study, 118 patients with burns between 75-75% of body surface area were studied. Patients were randomly divided into two groups. In the first group, patients were not satisfied with the preparation of xenoderm and were treated by traditional methods. In the second group, patients were satisfied with the preparation of xenoderm and the treatment of burns was performed by biological dressing.

Results: The mortality rate in the traditional method (53 patients) was 19 (35%) and in the biological dressing method (65 patients) was 7 (10.8%) ($p = 0.001$). If the deceased were excluded, the mean length of hospital stay was 31.3 days in the traditional group versus 18.2 days in the biological dressing group ($p = 0.0005$), the number of dressings in the traditional group was 22.1 vs. 9.9 in the biological dressing group ($p = 0.005$).

Conclusion: The results of this study show that biological dressing increases patient survival, reduces hospital stay and reduces daily extensive dressings. A randomized clinical trial study is recommended.

Keywords: Pig skin, Xenoderm, Extensive burn, Biological dressing, Early excision

Covid-19 and cardiovascular system (Review)

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Introduction: SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) and coronavirus disease (COVID-19) has become a serious global threat to public health in a short time, since the first case was reported at the end of 2019, in China. Infected patients show a variety of symptoms. These symptoms include fever, cough, fatigue, sputum production, shortness of breath, myalgia or arthralgia, sore throat, headache, and diarrhea. Although most clinical presentations are related to the respiratory system, the disease may also affect the cardiovascular system. I investigate the effect of covid-19 on the heart and cardiovascular system in this review article.

Methods: In this review study, three databases include Google scholar, pub med, and Science direct; and keywords like COVID-19, SARS-COV-2, cardiovascular system, heart, and arrhythmias used for collecting the articles. I reviewed all articles and removed those were not relevant to the study domain from the study process.

Results: Besides the respiratory system, angiotensin-converting enzyme 2 (ACE2) is expressed in the human cardiovascular system (such as the heart) and SARS-CoV-2 may cause myocardial damage or other damages by several mechanisms. SARS-CoV-2 infects humans by using the spike protein to bind to the ACE2 receptors on the surface of the myocardial cell membrane. Animal studies have shown that cellular ACE2 levels decrease due to SARS-CoV infection and also affect cardiomyocytes and conduction system disease. It has been reported that patients with the SARS-CoV infection experience different cardiac manifestations, including arrhythmias and sudden death. Sinus bradycardia, sinus tachycardia, and atrial fibrillation were the most common cardiac arrhythmia observed in patients with COVID-19 infection according to reports and one survey. Further, other arrhythmias, including atrial and ventricular arrhythmias, have been observed in COVID-19 patients, without any history of arrhythmia. Arrhythmias in COVID-19 can be caused by myocarditis, hypoxia, or abnormal host immune response, and secondarily as a result

of myocardial ischemia, myocardial strain, autonomic imbalance, electrolyte disturbances, intravascular volume imbalances, and drug side effects. Arrhythmias are not just because of the direct effect of COVID-19 infection, but probably as a result of systemic illness.

Conclusion: Although respiratory distress is the most important symptom of COVID-19, cardiac complications have also been reported in patients with COVID-19. The cardiac complications include heart failure, myocarditis, and acute coronary syndrome. There is several evidences showing that arrhythmias are also one of the major complications. It is necessary to increase the awareness of interactions between drugs, monitor electrocardiogram (ECG), and provide special considerations for patients with COVID-19 to manage arrhythmias and other heart diseases.

Keywords: COVID-19 , SARS-COV-2 , cardiovascular system , heart, , arrhythmias

CRISPR/Cas9 gene editing technology and its application to the coronavirus disease (COVID-19) (Review)

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Introduction: CRISPR gene editing is a genetic engineering technique in molecular biology by which the genomes of living organisms may be modified. It is based on a simplified version of the bacterial CRISPR-Cas9 antiviral defense system. By delivering the Cas9 nuclease complexed with a synthetic guide RNA (gRNA) into a cell, the cell's genome can be cut at a desired location, allowing existing genes to be removed and/or new ones added in vivo (in living organisms). Clustered-Regularly Interspaced Short Palindromic Repeats (CRISPR), and CRISPR associated (Cas) protein (CRISPR/Cas) structures were first identified in E. coli in 1987 and guard prokaryotic cells from any invading pathogens, harmful events and plasmids by recognizing and cutting foreign nucleic acid sequences that contain short palindromic repeats spacer sequences. Several genome editing approaches have been developed based on these mechanisms; the most recent is known as CRISPR/Cas. Before the CRISPR technique was revealed in 2012, editing the genomes of plants and animals took many years and cost hundreds of thousands of dollars.

Methods: By reviewing the latest scientific articles, the PubMed site and scientific books have been collected.

Results: CRISPR/Cas has attracted significant interest in the scientific community, especially for disease diagnosis and treatment, as it is quicker, less expensive and more precise than other genome editing approaches. The evidence from gene mutations in specific patients generated using CRISPR/Cas can assist in the prediction of the optimal treatment schedule for individual patients and for innovation purposes in other researches like replication in cell culture of coronaviruses like severe acute respiratory syndrome coronavirus-2 (SARS-CoV2 or COVID-19).

Conclusion: CRISPR gene editing is considered highly significant in biotechnology and medicine as it allows for the genomes to be edited in vivo with extremely high precision, cheaply and with ease. It can be used in the creation of new medicines, agricultural products, and genetically

modified organisms, or as a means of controlling pathogens and pests. It also has possibilities in the treatment of inherited genetic diseases as well as diseases arising from somatic mutations such as cancer.

Keywords: CRISPR gene editing, CRISPR-Cas9, guide RNA (gRNA), COVID-19, replication

Cytotoxic activity of Prodigiosin of Serratia marcescens on cancer cells (Review)

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Introduction: Cancer and malignancies are the main cause of fatalities for decades around the world. Some apoptosis-targeting drugs have been recently developed against tumor cells with great potential for cancer therapy. Prodigiosin (2-methyl-3-pentyl-6-methoxyprodigiosene = PGA) is a natural red pigment produced by Serratia marcescens comprises a common 4-methoxy, 2-2 bipyrrole ring which induces apoptosis in different types of cancer cells with low toxicity on normal cells. Recent studies have focused on the effect of prodigiosin on the apoptotic-related gene expression in various human cancer cells, such as human breast cancer (T47D) and human colon adenocarcinoma (HT-29) cells. Malignant cells have been treated with different prodigiosin concentrations and different molecular and cellular methods have been used for evaluating Caspase 3 activation and apoptosis.

Methods: .

Results: Therapy of the cells via expanding prodigiosin concentrations remarkably reduced the growth of cells in a time and dose-dependent manner. The amount of proapoptotic markers, such as caspase-3, Bax, and Bad mRNA versus the amount of anti-apoptotic markers, such as Survivin, and Bcl-2, specifies the cell resistor to apoptosis after exposure to prodigiosin. The levels of Survivin protein are controversary to the levels of caspase-3 protein in a cell. Low Survivin levels with high caspase-3 protein levels showed a correlation with higher rates of apoptosis in treated cells while the MMP-9 protein levels, involved in the development of several human malignancies, showed an inverse relationship with levels of caspase-3 protein. Low protein levels of MMP-9 with high caspase-3 protein levels showed a correlation with higher rates of apoptosis in cells

treated with prodigiosin. Furthermore, the results illustrated that prodigiosin treatment is able to decrease Bcl-2, anti-apoptotic proteins, expression at demonstrated concentrations in comparison with untreated cells. Compared to Bcl-2 mRNA and Survivin levels, prodigiosin increased the expression of the Bad and Bax genes. Caspase-3 activation was significantly enhanced along with a rise in the prodigiosin doses in the treatment of tumor cells.

Conclusion: The intestinal microbiota of insects has become a key area of interest in recent years. One of the bioactivity secondary metabolites produced by Serratia marcescens is recognized for its capability of generating plenty of secondary metabolites. It has been demonstrated that there is a relationship between prodigiosin and inhibiting the growth of cancer cells by apoptosis induction mechanism. Therefore, prodigiosin could be used in the new generation of anticancer factors. Finding the prodigiosin mechanism on apoptosis induction and recognition of its molecular spot could provide valuable insight into its available applications in cancer therapy and benefit. However, the function of prodigiosin in apoptosis mechanisms needs further research.

Keywords: Prodigiosin _ Serratia marcescens _ Cytotoxicity _ apoptosis_ anticancer

Detection of CDT toxin genes in Campylobacter spp. (Research Paper)

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Introduction: Campylobacter subspecies represent a highly frequent cause of foodborne gastrointestinal (GI) illnesses in humans worldwide. The incidence and prevalence of campylobacteriosis due to infection with Campylobacter jejuni and campylobacter coli has increased over the past decades, both in developed and developing countries. The clinical outcome of C. jejuni and C.coli infection ranges from mild to severe diarrheal disease, and some postinfection sequelae, including Guillainâ€“BarrÃ© syndrome, reactive arthritis, and others. Several genes have been linked to Campylobacter virulence, but the most important are cytolethal distending toxin (cdt), which disrupts mucosal Â¬barriers by causing host cell death. Cytolethal distending toxin (cdt) in Campylobacter spp. is among the significant virulence factors of these bacteria in the intestine.

Methods: Campylobacter detection in the present study was pre-treatment- Kapandis Baseri (prÃªt-KB) technique and the medium was blood and antibiotic free Kapandis Baseri (KB) medium (HiMedia, Mumbai, India). To perform the method faecal samples were added (10% (w/v)) in sterile phosphate-buffered saline (0.1 mol l-1, pH 7) (Merck, Germany) to obtained 10% suspension. The suspension was centrifuged at 8500 rpm for 10 min, then it was placed at room temperature. Afterward 10â€“15 min, 0.1 ml supernatant from the tube was plated on the KB medium (HiMedia, Mumbai, India). The plates were incubated at 37Â°C for 48 h in microaerophilic conditions and tested daily for 5 days. All suspected colonies grew on the KB medium confirmed by typical morphology, darting motility, gram staining, oxidase, and catalase tests. The isolates with presumptive Campylobacter character were subjected to standard Campylobacter phenotypic identification tests recommended by Atabay and Corry . These tests included H2S by lead acetate strip, nitrate reduction, growth in 1% glycine and 3.5% NaCl, growth at temperatures 25Â°C, 37Â°C, and 42Â°C, hippurate hydrolysis, indoxyl acetate hydrolysis, urease production, and resistance to Nalidixic acid (30 Î¼g) and Cephalothin (30 Î¼g). Additional tests for identification of Campylobacters

were alkaline phosphatase production, oxidative-fermentative test (OF Test), and glucose fermentation. All items used in the phenotypic identification tests were purchased from Parsalab (Tehran, Iran). At the end, the PCR method was carried out in order to confirm the phenotyping results and detection of cdtA, cdtB and cdtC genes. The PCR assay was done for authentication of Campylobacter and detection of cdtA, cdtB and cdtC genes. DNA was extracted from suspected colony using phenol chloroform method. The PCR was performed in 25 ml of the reaction mixture with a final concentration of 1Ã—PCR reaction mix, 10pgâ€“1Î¼g concentration of template deoxynucleotide triphosphate (DNA), 0.1 â€“1 Âµmol L-1 concentrations of each primer (Macrogen, Inc, Seoul, Korea), 3.2 m mol L-1 MgCl2 solution, and 1.25â€“2.5 U/50 Î¼l of GoTaq DNA polymerase. All items used in the PCR were purchased from Yekta Tajhiz Azma (Tehran, Iran) and the experiment was performed by thermal cycler (Bio-Red, Singapore). A 100-bp DNA ladder (Yekta Tajhiz Azma, Tehran, Iran) was used as a DNA molecular ladder. PCR products were electrophorized using 1% agarose gel (Yekta Tajhiz Azma, Tehran, Iran) at 80 V for 60 minutes. In addition detection of cdtA, cdtB and cdtC genes from each DNA extract was carried out and all amplified DNAs were visualized with UV transilluminator (Heidolph, Germany).

Results: Sampling from the poultry faeces was conducted between May 2020 and September 2020 in behbahan city, khuzestan province, iran. The results obtained indicated that 27 strains of Campylobacter spp. were isolated. Among the 27 Campylobacter strains, including 22 Campylobacter jejuni and 5 Campylobacter coli, the prevalence of cdtA, cdtB, cdtC, virulence genes were 40.74% (11/27), 85.19% (23/27), 77.77% (21/27), respectively

Conclusion: The research works on the virulence characteristics of potentially pathogenic bacteria in domestic animals and in foods containing animal origin are essential for the safety of the user. Although for assessing campylobacteriosis risk, heterogenic identification and virulence of genes of Campylobacter species isolated from the faeces samples of poultry are needed, so far it has not been done in the Khuzestan province. The results of our study showed that over 80% of the Campylobacter isolates have genes interfering in toxin production (cdtB), which signifies that most of the Campylobacter isolates have powerful pathogenic .

Keywords: Detection, CDT toxin genes, Campylobacter spp.

Detection of tetracycline antibiotic based on reaction with TetX monooxygenase (Review)

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Introduction: Tetracyclines are broad-spectrum antibiotics used against gram-positive and gram-negative bacteria. Tetracycline binds non-covalently to the ribosome, which inhibits aminoacyl-t RNA binding to the ribosomal receptor site, thereby inhibiting protein synthesis. Increased use of this antibiotic in food products such as milk, meat, poultry causes negative effects on human health. Examples of these side effects include: allergic reactions, increased resistance to antibiotics, liver damage. Some farmers add antibiotics such as tetracycline to milk for various reasons, including diseases of the mammary glands of cows or lack of hygiene in milk collection workshops. Antibiotics added to milk have an inappropriate approach for both the producer and the consumer. For example, in the production process, the presence of this substance leads to the lack of growth and activity of beneficial bacteria in milk processing, which as a result of the final product does not have the appropriate quality and rheology and the consumer suffers poisoning. Methods such as microbiological assay, ELISA, HPLC, LC / MS, CE are used to identify tetracycline antibiotics, but these methods require complex and expensive tools and it takes a long time to detect this analyte with these methods. Therefore, the development of rapid detection methods for tetracycline antibiotics is very important .The development of diagnostic method based on the interaction between TetX monooxygenase enzyme and tetracycline is an effective step in the rapid detection of this analyte.

Methods: In this study, the effect of TetX2 monooxygenase enzyme on tetracycline antibiotic was investigated in order to evaluate rapid tetracycline measurement methods.

Results: TetX is a FAD-dependent monooxygenase that degrades a wide range of tetracycline analogues. TetX2 monoxygenase is isolated from the CTnDOT transposite contained in Bacteroides thetaiotaomicron. The molecular weight of this enzyme is 44 kDa, which catalyzes the selective hydroxylation of TC to 11 a-hydroxytetracycline through the participation of NADPH as a factor and O2 as an electron receptor.

Conclusion: Therefore, the reaction between TetX2 and tetracycline enzymes leads to the development of enzyme-based biosensors for rapid detection of tetracyclines.

Keywords: Tetracycline, Biosensors, TetX2 monoxygenase, Antibiotic

Different formulations of inactivated COVID-19 vaccine candidates in the human compatible adjuvants: Preclinical studies in mice (Research Paper)

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Introduction: The Covid-19 pandemic started in December 19 in Wuhan (China). The World Health Organization named the epidemic a Public Health Emergency of Global Importance in January 2020 and a pandemic in March 2020. Numerous vaccines are currently being developed using various methods such as inactivated vaccine, recombinant protein vaccine, live attenuated vaccine, adenovirus vector vaccine, DNA vaccine and mRNA vaccine. Adjuvants are an important component of inactivated vaccines and elicit specific immune responses that have higher resistance and durability. Here, we first isolated and inactivated the human COVID-19 virus and then different formulations with Alum, Montanide 51VG and Montanide 720VG adjuvants were developed and then examined different aspects of the immune response.

Methods: A SARS-CoV-2 strain was isolated and cultivated in Vero cell line for propagation, and the virus was inactivated with formalin. Inactivated COVID-19 virus was formulated in Montanide ISA 720VG, Montanide ISA51VG and or Alum hydroxide adjuvants. Inactivated COVID-19 virus in PBS buffer was admixed with Montanide ISA 720VG (30/70) and Montanide ISA 51VG (50/50) by vigorously shaking and homogenized using homogenizer. For Alum-based vaccine, 4Âµg of inactivated COVID-19 virus in PBS buffer was mixed with 200Âµg of Alum hydroxide adjuvant and shaked at 100 RPM for 60 minutes and allowed that the viral particles adsorb on the surface of Alum gel. Six-to eight-week-old male BALB/c mice (N=40) were purchased from Royan Institute of Iran (Tehran, Iran) and grouped as below; Group 1: inactivated COVID-19-Alum vaccine. Group 2:

inactivated COVID-19-Montanide ISA-51VG vaccine. Group 3: inactivated COVID-19-Montanide ISA-720VG vaccine. Group 4: Mice were immunized with PBS as control group. Experimental mice were immunized subcutaneously with 4Âµg of vaccine, two times on days 0 and 14 and two weeks after the final immunization, immunologic parameters were assessed.

Results: Immunization with COVID-19-Montanide ISA51VG shows a significant increase of IFN-Î³ cytokine versus COVID-19-Alum, COVID-19-Montanide ISA720VG and control groups (P< 0.0033). The results of IL-4 response show that injection of COVID-Alum showed a significant increase versus COVID-19-Montanide ISA 51 VG, COVID-19-Montanide ISA 720 VG and control groups (P<0.0206). The results of CTL activity based on Gr-B secretion showed that immunization with COVID-19- Montanide ISA51 VG and with COVID-19-Montanide ISA720 VG resulted to a significant increase versus COVID-19-Alum and control groups (P<0.0075). Results of specific IgG titer in the experimental groups showed that immunization with COVID-19- Montanide ISA51 VG and with COVID-19-Montanide ISA720 VG resulted to the highest IgG titer and a significant increase versus COVID-19-Alum and control groups (P<0.0143). Results of specific IgG-1and IgG2a level showed that all three formulations of COVID-19-Alum, COVID-19-Montanide ISA51VG and COVID-19-Montanide ISA720VG vaccine showed a significant increase versus the control group (P<0.0001).

Conclusion: According to the immune responses triggered by different formulations of COVID-19 in the human compatible adjuvants, it seems that the type of vaccine formulation is a critical parameter that effect on the cellular and humoral immune responses and vaccine potency. Here, results showed that human compatible oil-based adjuvants were more potent than Alum adjuvant in the induction of cellular and humoral immune responses versus COVID-19 virus.

Keywords: Inactivated COVID-19, Alum, Montanide 51VG and Montanide 720VG, Adjuvants, Vaccine formulation.

Disorders of Long Non-Coding RNAs (lncRNA) in Neurodegenerative Diseases of the CNS (Review)

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Introduction: Introduction: The development and homeostasis of the central nervous system (CNS) are controlled by epigenetic mechanisms. These mechanisms modulate gene activity and enhance the selective arrangement of functional gene networks in the neural terminal response to the complex activities of environmental signals. Therefore, it is not surprising that disorders in the epigenetic process cause a range of mental and neurological disorders. Epigenetic mechanisms include DNA methylation and a variety of histone changes controlled by long non-coding RNAs. While the biological functions of many lncRNAs have not yet been fully elucidated. But recent research shows that lncRNAs play a key role in determining cellular identity. This function seems to be important for the arrangement of glial cells and nerve neurons in the CNS.

Methods: This review performed by searching lncRNAs, neurodegenerative diseases of the CNS, and epigenetic mechanisms keywords in various internet databases such as PubMed, and Google Scholar.

Results: The results showed recognition of the factors affecting the activity and function of lncRNAs in the CNS, followed by epigenetic changes.

Conclusion: Conclusion: Also in this article tries to address the factors that disrupt lncRNAs as one of the important factors in various CNS pathologies including neurological disorders and diseases, neuro-immunological problems and nerve growth, primary brain tumors, and mental illnesses. Recognition of pathogenesis and factors affecting these diseases can be used for therapeutic purposes.

Keywords: Keywords: lncRNA, Epigenetic Mechanisms, Neurological Disorders, CNS

Disturbed Metabolic Pathways in the Neuro-Immune Disorder of MS (Review)

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Introduction: Multiple Sclerosis (MS) is one of the most common causes of neuro-immune disability that can severely affect a patient's life. More than 2.5 million people worldwide have MS, and that number is rising dramatically. The etiology of MS is still unknown, but empirical evidence suggests that both genetic and environmental factors play a role in the disease. Various methods have been used, including the GWAS method and GO analysis on genes affecting the pathogen MS. These studies have shown that metabolic processes and several signaling pathways play an important role in MS.

Methods: This review performed by searching keywords of MS, impaired metabolic pathways, defects in lipid and myelin metabolism of nerve cell membranes, and pyruvate defects in various internet databases such as PubMed, Google Scholar, and Scopus.

Results: The results showed the recognition of disturbed metabolic pathways in MS.

Conclusion: In this article we have tried to investigate the disturbed metabolic pathways in MS that play an important role in this disease. These pathways include the disrupted pathway related to the factor that regulates glucose and lipid metabolism, the disrupted pathway related to the maintenance of complement and proper content of lipids and myelin in nerve cell membranes, as well as defects in pyruvate metabolism. Therefore, by targeting these metabolic pathways, more effective drugs can be achieved in relation to MS.

Keywords: MS, Metabolic pathway, Myelin, Nerve membrane lipid, Pyruvate

Druggability of Cavity Pockets within SARS-CoV-2 Spike Glycoprotein and Pharmacophore-based Drug Discovery (Research Paper)

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Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent of the current COVID-19 pandemic. Researchers identified several viral proteins in SARSâ€CoVâ€2 as therapeutic targets, including S protein, envelope (E) protein, membrane (M) protein, nucleocapsid protein (N), proteases (3C-like protease (3CLpro), papain-like protease (PLpro)), Nsp1, Nsp3 (Nsp3b, Nsp3c, Nsp3e), Nsp7 Nsp8 complex, Nsp9â€“Nsp10, and Nsp14â€“Nsp16, ORF7a, helicase, RNA-dependent polymerase (RdRp) [10,11]. Among them, the S protein gained more attention due to its role in the entry of the virus. S protein contains two domains S1 and S2 [12]. The S1 domain has a significant role to play in virus entry.Virus spike glycoprotein is a good target for drug discovery. The purpose of this research was to examine the potential for druggability of Spike protein for pharmacophore-based drug discovery.

Methods: Predicted 3D viral protein structure was investigated in druggable cavities using CavityPlus. A pharmacophore was extracted from the druggable cavity and used for hit identification. Autodock Vina was used to evaluate the affinities of match hits for lead identification. A chemical library was also built from the chemical backbone to optimize the lead compound.

Results: 42 cavities were found within the virus Spike glycoprotein and five of them were druggable .The druggable cavity No.1 with highest Drug score (10041) was selected for pharmacophore modeling. Ten druggable cavities were found within the glycoprotein spike. Only one cavity with the highest score at the binding site was selected for pharmacophore extraction. Hit identification of a virtual library containing more than 1 billion natural product compounds resulted in the identification of 410 hits. One chemical (Compound38) was found to have the highest affinity to SARS-CoV-2. Drug-likeness and ADME properties of the chemical library

was predicted by SwissADME [31] and is provided in the supplemented materials . Accordingly, no significant toxicity was observed.

Conclusion: this study provides a druggable region within viral glycoprotein and a candidate compound to block viral entry.In the first place, this study provides a comprehensive search for significant drug-gable cavities within SARS-CoV-2. Second, a virtual library containing millions of natural products has been screened. Third, chemical candidates were developed to block viral entry by interacting with the binding domain of viral spike glycoprotein. The findings of the study presented may be used in future studies on COVID-19 therapy.

Keywords: SARS-CoV-2; COVID-19; Spike protein; Virtual screening; Docking

Easy Method for the Detection of Cellulases from Halophilic Bacteria on Agar Plates Using Gramâ€™s Iodine (Research Paper)

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Introduction: The term â€˜â€˜cellulasesâ€™â€™ refers to a group of enzymes that catalyze the hydrolysis of cellulose into sugars. Cellulolytic microorganisms play an important role in the biosphere by recycling cellulose, the most abundant carbohydrate produced by plants. Cellulolytic enzymes from microorganisms also have many potential biotechnological and industrial applications. Cellulases are required in large quantities because of their application in many industries, such as textiles, detergent, food, animal feed, bio-fuel, paper and pulp, pharmaceutical, and waste management. The first step in the development of the industrial process for the production of an enzyme is to isolate the potential strains. Isolation and screening of microbes for cellulases are of immense importance keeping in view of the demand for new enzymes and the improvement of their biotechnological applications. An easy, fast, and environmentally friendly qualitative method is described for screening microorganisms producing extracellular cellulase on the agar plate.

Methods: Soil samples were collected from Howz-E Soltan Salt Lake of Iran, for the isolation of bacteria-producing cellulases. Samples were transported to the laboratory and stored at 4C until used. Five-fold serial dilutions of each soil sample were prepared in sterilized distilled water, and a 0.1 ml diluted sample was spread on the surface of nutrient agar medium with NaCl 20% (pH 7.4). Plates were incubated at 30C for 48 hours for bacteria. Morphologically different colonies appearing on the plates were purified on the respective medium for bacteria. The purified isolates were preserved at 4C and used during the course of the study.

Results: As a result, The two bacterial isolates T1 and H1-1 producing cellulase were identified as Metabacillus halosaccharovorans sp. based on

partial 16S rRNA gene sequencing. The observation on the development of cellulose clearance zone showed Gramâ€™s iodine to be more effective compared with Congo red plus 1 M NaCl for screening and qualitative estimation of cellulase production by microorganisms on CMC agar plates. There was difficulty in differentiating the enzyme-lysed zone from the CMC-containing area in the plates flooded with these reagents. Moreover, there was a waiting period of at least 5 to 10 minutes for the development of clearance zones. Interestingly, the plates flooded with Gramâ€™s iodine showed distinct, clear, and prominent zones of clearance around the colonies showing cellulase production with bluish-black coloration in the nonhydrolyzed part of the medium. It took only 5 minutes for the development of clearance zones after flooding. There is a possibility that the added Congo red could have affected growth and cellulase production by the isolates because of its harmful effects. However, a sharp increase in the color contrast of the hydrolyzed zone and nonhydrolyzed portion of the medium is obtained on flooding with Gramâ€™s iodine because it further enhanced the appearance of the already sharply discernible clearance zone by producing a bluish-black complex with cellulose (polysaccharide) and not with the glucose (monosaccharide). This new method for assaying has the double advantage of being quick as well as based on nontoxic chemicals.

Conclusion: The present studies showed that the use of Gramâ€™s iodine remarkably enhances the sharpness of the clearance zone, making the process for screening cellulase-producing microorganisms easy, efficient, and rapid. Although the new method is a qualitative assay, the greatest advantage lies in its simplicity, quickness of performance, and effectiveness for screening a large number of microorganisms. Moreover, it avoids the use of toxic chemicals.

Keywords: Halophiles, Screening, Isolation, Cellulase, Staining

Evaluation and analysis of synthetic HIV-1 V3 peptides incorporation with C3d adjuvant and vector design to increase the peptide expression (Research Paper)

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Introduction: One of the main sites for the production of neutralizing antibody against HIV-1 is the Glycoprotein 120 V3 region. According to the previous studies, the C4-V3 T303-E22C and the C-PRILGPG-C sequences are designed and produced as synthetic peptides that showed a suitable potential in triggering immunogenic properties against HIV. This study aims to investigate the variability of the second and third structures of these designed synthetic peptides after adding C3d adjuvant for increasing the level of immunogenicity. Additionally, a suitable vector has been designed for expressing the fusion proteins.

Methods: After designing different arrangements of synthetic peptides with C3d adjuvant and linker, we have used Phyre2 (intensive format) and Raptorx software for homology modeling and predicting the second and third structures of fusion proteins. The stability and half-life Evaluation of designed peptide sequences applied by Protparam and Rampage software. For determining the secondary structure of RNAs obtained by expressing the nucleic acid units of our designed peptide sequences and its âˆ†G amount the M Fold software has been used. The location of fusion protein sequences and the type of expression host determined via PSort Prediction software.

Results: The prediction of the second and third structures of fusion proteins showed the junction of C3d adjuvant to the beginning of the C-PRILGPG-C sequence (without linker) and the end of the C4-V3 T303-E22C (with a linker) had more similarity with the primary structure of these proteins.

Conclusion: Due to the placement pattern of synthetic peptide sequences at the beginning and end of the C3d adjuvant peptide, the possibility of simultaneous binding of these two peptides to the adjuvant was possible without affecting the primary structures of both synthetic peptides.

Additionally, our findings from Protparam analysis revealed that for expressing the C4-V3 T303-E22C fusion protein the mammalian Eukaryotic cell host is needed while expressing the C-PRILGPG-C fusion protein is suitable with both Prokaryotic and Eukaryotic cell host. Eukaryotic expression vector pGA was designed to express the fusion of proteins of this study.

Keywords: Keywords: HIV1, Antibodies, Neutralizing, Adjuvant, Peptides

Evaluation of analgesic and anti-inflammatory effects of hydroalcoholic extract of Lavandula angostifulia in male rats (Research Paper)

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1.
2. Neuroscience

Introduction: Evaluation of analgesic and anti-inflammatory effects of hydroalcoholic extract of Lavandula angostifulia in male rats

Methods: Hydroalcoholic extract of lavender stems and leaves was extracted by soaking method and saline was used as a solvent. This extract was prepared in doses of 100, 200 and 400 mg / kg and was injected intraperitoneally to rats weighing approximately 200-400 g. The mentioned groups along with the control group and the solvent group were subjected to heat test (tail-flick) and inflammation caused by formalin soles.

Results: The hydroalcoholic extract of lavender reduced the inflammation caused by formalin soles, which was significant in all doses, but was more effective at 400 and 200 mg / kg than the control and solvent groups ($P<0.001$). The extract also caused pain in the thermal pain test (tail-flick) at doses of 200 mg / kg and 100 ($P<0.001$) and also significantly reduced pain at a dose of 400 mg / kg ($P<0.001$).

Conclusion: According to lavender studies, this plant contains a large amount of vitamin C and other antioxidants that probably reduce ROS, increase the level of antioxidant enzymes such as superoxide dismutase, glutathione peroxidase and catalase and can inhibit the synthesis of Nitric oxide. Lavender contains a large amount of substance called Linalool which is considered as an antagonist of NMDA receptors and may reduce neuropathic pain induction by inhibiting the activity of these channels.

Keywords: Thermal pain,Chemical pain,Edema,Lavender,Hydroalcoholic extract

How Plant Molecular Farming Can Help Fight Against COVIDâ€19? Rev. 01 (Review)

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Introduction: Abstract Severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) is a new virus responsible for the COVID- 19 pandemic, which is the worst public health crisis of this Century. Urgent measures are needed to contain and control the virus, particularly diagnostic kits for detection and surveillance, therapeutics to reduce mortality among the severely affected, and vaccines to protect the remaining population. Some scientists working on plant biotechnology together with commercial enterprises for the emergency manufacturing of diagnostics and therapeutics have aimed to fulfill the rapid demand for SARSâ€CoVâ€2 protein antigen and antibody through a rapid, scalable technology known as transient/stable expression in plants. Plant biotechnology using transient/stable expression offers a rapid solution to address this crisis through the production of lowâ€cost diagnostics, antiviral drugs, immunotherapy, and vaccines. Transient/stable expression technology for manufacturing plant based biopharmaceuticals is already established at commercial scale. Here we discuss the potential role of plant molecular farming in the rapid and scalable supply of protein antigens as reagents and vaccine candidates, antibodies for virus detection and opinions regarding how plan molecular farming can help fight against COVIDâ€19. The COVID-19 pandemic is an urgent global health crisis in human history, which has dramatically affected the health, economy, and social mobility of almost everyone on the planet. The emergence of SARS-CoV-2 in late 2019 and its rapid spread in 2020 has posed several global challenges that demand new solutions in public healthcare and the biomedical research ecosystem (Webb et al., 2020). The normal life and livelihood of most world citizens have been disrupted, causing an incalculable economic depression. Health officials and government agencies have imposed extreme measures to limit human mobility and social distancing strategies to slow down the infection rate, thus decreasing the total number of hospitalized patients at one time. This strategy also allows more time to find and develop effective testing reagents to identify carriers, find suitable antiviral drugs to treat severely

affected patients, and develop a vaccine to protect the unexposed portion of the population. During this crisis, plant scientists can play a key role in developing new diagnostics reagents and therapeutics with their knowledge and plantâ€based biopharmaceuticals infrastructure. In this article, we discuss how plant molecular farming could provide practical solutions to address the outbreak of COVID-19. The World Health Organization (WHO) welcomes innovations around the world including repurposing drugs, traditional medicines and developing new therapies in the search for potential treatments for COVID-19. use of plants for the large-scale production of biopharmaceuticals (Molecular farming) represents an interesting and mature technology that has already proved its benefits in terms of safety, scalability, rapidity and reduced manufacturing costs. Monoclonal antibodies (mAbs) are useful tools in medicine, biology and biochemistry due to their binding specificity to different molecular targets and their stability both in vivo and in vitro. Mammalian cell cultures mainly based on Chinese Hamster Ovary cells (CHO) are still the favored system for the production of commercial mAbs, even if the increasing demand (also linked to the growing market) is promoting the development of alternative expression platforms. Indeed, the facilities necessary for large-scale production in mammalian cells require high initial investments and their operating and maintenance costs are high (Ecker et al., 2015). Among alternative expression systems, plants represent promising bioreactors for the large-scale production of recombinant proteins and antibodies. They offer an attractive expression platform with several advantages such as the absence of potential human pathogens, possibility to engineer a tailored antibody glycosylation profile, possibility to scale-up production by simply increasing the number of plants and competitiveness of manufacturing costs.

Methods: Molecular Farming and the Plant-based Vaccines Technology Post-translational modifications of proteins occurring in plant cells are essentially similar to those in animal cells and the correct assembly of complex molecules, such as antibodies, are assisted by chaperones that mediate the folding and formation of disulfide bonds while the addition of N-glycans is performed by specific cellular glycosyltransferases. Plant molecular farming encompasses a variety of different expression technologies, ranging from stable nuclear transformation (transgenic plants) or plastid transformation (transplastomic plants) to transient expression without stable transgene integration (Fischer and Buyel 2020). Transient or epichromosomal transformation differs from stable

transformation in that the exogenous sequence is not inherited by the progeny thus reducing the risk of environmental biosafety issues linked to the dissemination of the transgene through seeds or pollen. This approach generally provides high protein yields in a very short period of time (few days to weeks) which is not achievable via stable transformation (Komarova et al., 2010). Transient expression can be obtained using either vectors or plasmids containing T-DNA gene cassettes derived from A. tumefaciens bearing a strong constitutive promoter or vectors carrying appropriately modified genomic sequences of plant viruses inserted in T-DNA cassettes (viral vectors) (Kopertekh and Schiemann 2017). Given the urgent need for diagnostics, vaccines, and therapeutics for a rapidly-spreading novel or re-emerging disease, only transient expression systems provide the necessary speed and scalability (TusÃ© et al., 2020). Currently, Agrobacterium-mediated transformation is the most popular method to achieve this modification since this bacterium has the ability to transfer large segments of DNA with minimal rearrangement at high efficiency with low number of insertions. Nonetheless, the transgene is randomly inserted into the genome, which often leads to positional effects that make expression levels unpredictable and interruption of endogenous genes a possibility. Another limitation is the induction of silencing mechanisms that hamper productivity. Nevertheless, it should be considered that new technologies are emerging to cope with these limitations by providing ways to achieve site-directed insertion through a number of mechanisms. Table 1: Description of the expression approaches for the production of plant-based vaccines and precedents for MERS/SARS-CoV-1 vaccines. Approach Attractive Features Drawbacks Proposed Target Antigens MERS/SARS Precedents Reference Stable nuclear genome transformation Inheritable antigen production, allows seed bank generation; post-translational modifications are performed; protocols available for several species including seed crops Non-site specific transgene insertion; horizontal gene transfer is possible; transgene expression affected by position effects and silencing; transformation takes long time S protein; multiepitope vaccines The N-terminal fragment of the SARS-CoV-1 S protein (S1) was expressed in stably transformed tomato and low-nicotine tobacco plants, which induced IgA and IgG responses in mice. (Pogrebnyak et al., 2005) Transient nuclear genome transformation Rapid production; high productivity; implemented at the industrial level Seed bank cannot be generated; requires purification of the antigen to eliminate toxic compounds from the host and ag-robacteria residues S protein; multiepitope vaccines A chimeric protein of GFP and amino acids 1-658 of

the SARS-CoV-1 S protein (S1:GFP) was transiently expressed in tobacco leaves and stably transformed in tobacco and lettuce. No immunization assays were performed The SARS-CoV-1 N protein was transiently expressed in Nicotiana benthamiana, which induced in mice high levels of IgG1 and IgG2a and up regulation of IFN-Î³ and IL-10 in splenocytes. A chimeric protein of GFP and the SARS-CoV-1 S protein was transiently expressed in tobacco plants. No immunization tests were performed. The SARS-CoV-1 M and N proteins were transiently expressed in N. benthamiana. The N protein was antigenic but immunogenicity was not assessed. (Li et al., 2006; Zheng et al., 2009; Demurtas et al., 2016) Using transient expression systems, plants may offer the only platform that can be used to produce diagnostics and therapeutics at a large scale in a few weeks, which is extremely relevant to the current pandemic situation, and they can be scaled up rapidly to address unforeseen and sudden demands. Possibilities to Develop Anti-COVID-19 Plant-based Vaccines In the last 20 years, plants have become vital competitors to bacteria, yeast, and mammalian cellâ€based production systems for biopharmaceuticals. Plants are highly efficient in producing proteins of varying complexity, serving as a bioreactor/mini factory for manufacturing proteinâ€based diagnostics and therapeutics. Plantâ€based biopharmaceutical production platforms exhibit agility, accuracy, and speed by eliminating the risk of mutation and contamination during production and significantly shortening production timelines. Plants have much to offer for fighting against COVIDâ€19. 1. Diagnostic reagents The effective management of COVID-19 requires an increase in diagnostic capacity, particularly the development, manufacture, and stockpiling of assays to detect the SARS-CoV-2 genome and/or antigens itself or the antibodies it elicits. Accurate antibody tests for COVID-19 require high-quality reagents, although differences between analytical and clinical sensitivity has not yet been defined for any test. The huge demand for diagnostic kits has highlighted not only the critical shortage of reagents (recombinant antigens and antibodies) but also the means to produce them. Plants have already been shown to produce SARS-CoV antigens (Demurtas et al., 2016). The nucleoprotein (N), transiently expressed in N. benthamiana, was recognized by sera from Chinese SARS-convalescent patients around the time of the 2003 outbreak. Furthermore, the full-length membrane (M) protein was produced in plants but not in bacteria due to unanticipated toxicity (Carattoli et al., 2005). This provided proof of principle that plants could be used as a robust, rapid and flexible production system for SARS diagnostic reagents, potentially allowing the development of

immunological assays for stockpiling in case of recurring SARS outbreaks (De Martinis et al., 2016). Due to its rapid spreading nature, the COVIDâ€19 pandemic has created a sudden huge crisis for diagnostics, and consequently caused severe shortage in the diagnostic reagents and materials to manufacture them. Currently, two types of diagnostics are in high demand. The first one is the antigen test to detect the virus directly and thus identify, separate, and treat the infected populations. The second one is the antibody test to detect the antibody produced against the viral infection and thus identify the infected, convalescent, and immune populations. There are two types of antigen tests: the first one based on the detection of viral genomic RNA, and the second based on the detection of viral proteins. In the RNAâ€based test, the virus is detected by quantitative reverse transcription PCR (RTâ€qPCR), for which we only need to synthesize geneâ€specific primers from the published genome sequence of SARSâ€CoVâ€2. However, a major problem with the RTâ€PCRâ€based test is the lack of a universal positive control; thus, there is a possibility of false positive or false negative results. This problem can be solved by developing plantderived virusâ€like particles (VLPs) as a universal positive control for the RTâ€qPCR test. (Figure 1) The glycosylation patterns of proteins that form VLPs can impact their immunogenicity and protective capacity. Interestingly, glycoengineering strategies have been successfully implemented for plants, which allows diversifying their application as hosts for the production of biopharmaceuticals. This is a relevant aspect considering that plants lack the ability to perform glycosylation, which is a characteristic of mammalian systems. For instance, plants perform beta1,2-xylosylation, core alpha1,3-fucosylation, and the addition of a second N-acetylglucosamine (GlcNAc) to the mannose core. Moreover, plant glycans lack Î² (1,4)-galactose and sialic acid, as well as bi-antennary N-glycans (Lerouge et al., 2009). Virusâ€like particles (VLPs) based on plant viruses represent an exciting prospect for vaccine development. VLPs mimic the original structure of virus, which allows them to be easily recognized by the immune system of the host. VLPs lack core genetic materials, which ensures an extra layer of safety, as they cannot replicate in humans, making them nonâ€infectious, and can be manufactured in huge quantities by transient expression in plants (Rybicki E. P. 2020) Figure 1. Developmental routes for plantâ€based diagnostics and therapeutics to address the COVIDâ€19 crisis. Blue arrows indicate transient expression; brown arrow indicates stable expression; olive green arrows indicate potential routes for diagnostics; and light green arrows indicate potential routes for

therapeutics manufacturing platforms. SARSâ€CoVâ€2: severe acute respiratory syndrome coronavirus 2; VLPs: virusâ€like particles. Some of these images were generated using Biorender (https://biorender.com/). Although plant-derived SARS-CoV-2 VLPs have yet to be reported, the feasibility of this approach has been demonstrated by the successful production of other coronavirus VLPs in insect and mammalian cells (Lu et al., 2007; Bai et al., 2008; Lokugamage et al., 2008). This suggests that SARS-CoV2 VLPs could be assembled in plants by co-expressing the M, E, and S proteins. Medicago announced a program to develop a VLPbased COVID-19 vaccine candidate in July 2020, combining their recombinant coronavirus virus-like particle (CoVLP) technology with adjuvants from GlaxoSmithKline and Dynavax Technologies for the phase I trial8. A VLP-based COVID-19 vaccine program has also been announced by iBio Inc.6 This company was established with funding from the United States Defense Advanced Research Projects Agency (DARPA) and was part of the Blue Angel initiative to establish centers for the rapid delivery of medical countermeasures in response to emerging diseases, as demonstrated by the production of 10 million doses of influenza vaccine in only 1 month using its plant-based9. 2. Vaccine Vaccines are the most economical and effective way to control and prevent any infectious disease. Therefore, the development of an appropriate vaccine against COVIDâ€ 19 is urgent. Recent investigations have demonstrated that SARSâ€CoVâ€2 structural proteins can stimulate neutralizing antibodies and enhance the CD4+/CD8+ T cell response (Shang et al., 2020). SARSâ€CoVâ€2 consists of four structural proteins. Among them, the N protein is highly conserved in the CoV family, whereas the M and E proteins induce a weak protective response (Figure 2), indicating that the N, M, and E proteins are unsuitable for targets vaccine candidates (Gralinski, and Menachery 2020). Therefore, the S protein is the main target for vaccine candidates. However, the S protein of SARSâ€CoVâ€2 is divided into the S1 and S2 subunits. S2 is membraneâ€spanning and highly conserved (99%) in the CoV family, whereas the S1 subunit shows only 70% individuality to other strains of human corona virus. Blocking viral entry to the host cells is a promising strategy to control infection, and most of the vaccines for the SARSCoV have targeted the S1 subunit for this reason (Du et al., 2009). Manufacturing subunit vaccines based on individual proteins, producing either virus subunit antigens or VLPs, is a safer and quicker alternative than vaccines developed through conventional approaches using inactivated or attenuated strains. Figure 2. Structure of the SARS-CoV-2 virus. The virus is formed by an envelope membrane associated with the following structural

proteins: spike protein (S), which mediates binding to the host cell receptors and considered a critical target for the induction of antibodies capable of neutralizing the virus; hemagglutinin-esterase dimer (HE), which acts as a potent mediator of attachment and destruction of sialic acid receptors on the host cell surface; a membrane glycoprotein (M), which is important to generate the virus; and the envelope protein (E), which adheres to the M protein to form the viral envelope. The viral structure also comprises a nucleocapsid protein (N) that, along with the RNA genome, produces the nucleocapsid. Many subunit vaccine candidates for pandemic or seasonal strains of influenza have already been developed by transient expression in the tobacco plant. Vaccine antigens were produced with a deconstructed vector based on the tobacco mosaic virus delivered by the agroinfiltration technique with Agrobacterium tumefaciens. This technology ensures uniformly high levels of target protein expression in Nicotiana benthamiana and can produce a maximum of 200 mg of protein per kg of tobacco leaves within 3 weeks just after receiving the corresponding sequences. From the CoV family, only one previous report demonstrated that the S1 subunit of swineâ€transmissible gastroenteritis coronavirus (TGEV) expressed in Arabidopsis thaliana transgenic lines produces recombinant antigenâ€elicited TGEVâ€specific antibodies in mice, indicating that immunogenic CoV antigens can be expressed and produced in plants (Gomez et al., 1998). The S protein of several avian, swine and murine coronaviruses, as well as the N-terminal fragment of the SARS-CoV S protein, have been produced successfully in transgenic maize, potato, tomato, or tobacco plants by classic Agrobacterium-mediated transformation, or by display on the surface of plant viruses, and in all cases the products induced an immune response following oral delivery (Tuboly et al., 2000; Bae et al., 2003; Lamphear et al., 2004; Zhou et al., 2004) or nasal delivery (Koo et al., 1999). However, transient expression is more suitable for the speed and scale of production needed to address a rapidly-spreading disease live COVID-19.

Results: Result

Conclusion: Conclusions The emergence of COVID-19 has led to a global emergency that demands the development of new biologics, especially vaccines, to counteract against this threat. In this scenario, a plant-made vaccine is a viable approach to rapidly respond to this need. The current expression technologies offer relevant paths for developing anti-COVID-19

vaccines. Plant Molecular Farming through transient/stable expression in plants offers an outstanding platform to produce biopharmaceuticals to fight against COVIDâ€19. Transient/stable expression in plants is a faster, cost effective, scalable, and flexible technology than traditional microbe, insect, or mammalian cellâ€based platforms because there is no need to establish stable culture cell lines or costly culture media, neither is there any need for an extra setâ€up for the scaledâ€up production except for the cultivation of more plants. Crop plants can be grown in diverse environments; therefore, biopharmaceuticals could be produced using already established infrastructures for agricultural production and the same distribution networks that exist for the supply of food and cereal seeds, without the need for a cold supply chain. Plant Molecular Farming has the opportunity not only to fight against COVIDâ€19 but also to create a perfect model that allows a rapid and intended response to any crises in the future.

Keywords: COVID-19, Plant molecular farming, recombinant proteins, transient expression

Identification of Potentially Therapeutic Target Genes Of Hepatocellular Carcinoma (Review)

Yalda Shaterian,[1,*]

1.

Introduction: Hepatocellular carcinoma(HCC)is the second leading cause of death among worldwide.In this study,researchist aimed to identify the molecular target genes and detect the key mechanism of HCC by analyzing gene expression profiles

Methods: All profiles were extracted from the Gene Expression Omnibus database.The identification of the differentially expressed genes(DEGs)was analyzed by the GEO2R method.Kyoto Encyclopedia of genes and Genomes(KEGG)pathway and gene ontology(GO)enrichment analysis performed database for integrated discovery,visualization and annotation.The miRNA-gene network and protein-protein interaction(PPI)network were correlated by the cytoscape software.The identified hub genes were testified for survival curve using the Kaplan-meier plotter database.

Results: Expression profiles(GSE84006,GSE14323,GSE14811)and two miRNA expression profiles(GSE40744,GSE36915)had 592 overlapped DEGs and a total of 51 common up-regulated DEGs and 201 down-regulated DEGs were obtained after gene differential expression analysis of the profiles(GSE87630,GSE84598,GSE89377).functional enrichment analyses indicated that these common DEGs are linked to a series of cancer events.In this studies finally identified 10 novel gene in the progression of HCC(PLK1,PRPCC,PRPF4,PSMA7,OIP5,ASPM,NUSAP1,UBE2C,CCNA2,KIF20A)

Conclusion: The results show that 10 novel genes could be potential biomarkers or therapeutic targets for HCC

Keywords: hepatocellular carcinoma;hub gene;ppi network;gene expression profile;bioanformatic analysis

Identification of miR-194 potential target genes and signaling pathways in the liver fibrosis (Research Paper)

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is one of the most common causes of chronic liver disease, ranging from steatosis to non-alcoholic steatohepatitis (NASH) with increased risk of fibrosis, cirrhosis, and cancer. Liver fibrosis is the excessive accumulation of extracellular matrix proteins, mainly collagen fibers. Activation of hepatic stellate cells (HSCs) from the quiescent state is responsible for the exceeding collagen production. Previous studies have reported the down-regulation of miR-194 in activated HSCs (aHSCs), but more shreds of evidence are needed for better understanding of the exact cellular and molecular mechanisms. Here, we aim to investigate the potential role of miR-194 down-regulation in liver fibrosis through its target genes.

Methods: We extracted the miRNA-target genes interactions (MTIs) of hsa-miR-194-5p from various databases, including miRTarBase and TarBase 8 for experimentally validated and Target scan, miRWalk, miRDB, and DIANA-microT for predicted MTIs. For more accurate results, we selected only the genes associated with NAFLD using the DisGeNET database (UMLS IDs â€œC0015695â€, â€œC0400966â€, and â€œC3241937â€). We constructed protein-protein interaction (PPI) network using STRING and

visualized it by Cytoscape software. Finally, we used the enrichR online tool to perform pathway and functional enrichment analyses.

Results: Our study identified a total of 27 and 207 genes in common for validated and predicted MTIs, respectively. After comparing to the DisGeNET database, 24 genes overlapped between target genes and NAFLD-associated ones. The PPI network identified 11 genes, including SMURF1, CAV1, TMED2, FBXW7, ACVR2B, YAP1, FOXA1, GOT2, IL10, IL6ST, and SYVN1, have interactions together, while the others were disconnected from the network. Also, SMURF1 had the most connections, with a degree score of 3. These genes are supposed to be up-regulated due to the down-regulation of miR-194. Pathway analysis revealed significant enrichment in the BMP, ALK1, Ubiquitin-mediated proteolysis, TGF-beta, Delta Np63, p53, and NOTCH signaling pathways in addition to Cytokine-cytokine receptor interactions in the activation of HSCs. We expanded the PPI network by adding ten more interactors, and the new pathway analysis showed that SKP1, BMP2, SMAD7, and SEL1L are also involved in the previous signaling pathways.

Conclusion: Collectively, our findings identified the miR-194 potential related genes and signaling pathways, which can be implemented to uncover the underlying mechanisms responsible for the activation of HSCs and progression of liver fibrosis.

Keywords: hepatic stellate cells, miR-194, MTI, PPI, signaling pathway

In silico analysis of hsa-miR-21-5p target genes and rs4648298 relation with Colorectal Cancer (Research Paper)

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Introduction: Colorectal Cancer (CRC), is the third most common type of cancer in the world. Colorectal Cancer listed as a genetic disease, Based on the researches miRNAs (small non-coding RNAs) and SNPs (single nucleotide polymorphisms) might develop the chance of being infected by Colorectal Cancer. this study has been done in order to diagnose a biomarker for early detection of this cancer. Based on the bioinformatics analysis of this research, hsa-mir-21-5p, which is located on chromosome 17 was selected.

Methods: To perform a wide range of bioinformatics analysis miRBase , miRTarbase , miRWalk , TargetScan , DIANA TOOLS, miRSNPdb, miRdSNP, miRNASNP, DAVID, GeneMANIA databases, GraphPad Prsim 8.0 , databases and R a programming language, were selected to obtain essential data about microRNA basis , validated and predicted target genes , genes' expression , SNP, signaling pathways and genes' interaction network.

Results: According to the hsa-mir-21-5p targets PI3K, Akt, MSH2, MSH6, TGFBR2, APC and p53 genes are considered as the most regular genes of PI3K, PI3K-Akt, MSI, Wnt and p53 signaling pathways of Colorectal Cancer which their similar pattern is clearly notable. Furthermore, in the bioinformatics analysis of this study, the occurrence of rs4648298 in PTGS2, showed to have a vital role in CDC disease process, but to understand the role of this SNP in CDC a wide range of surveys are required.

Conclusion: According to PI3K-Akt signaling pathway, some genes containing Akt, PI3K seem might lead to metastasis via causing cell proliferation, cell cycle. Moreover, in p53 signaling pathway, p53 gene which activates via a cascade of genes, is able to uncontrolled proliferation, increased survival and Genomic instability. Thus, inhibition of these genes

by hsa-mir-21-5p that lead to metastasis and proliferation, mentioned miRNA is considered to be tumor suppressive.

Keywords: Bioinformatics, miRNA, SNP, CRC, Signaling pathways

In vitro modeling of disease as a paving road into personalized medicine: with an eye to COVID19 (Review)

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Introduction: Understanding the individual cellular and molecular mechanisms of human diseases plays a significant role to develop novel and improved therapies or the rapid diagnostics. In this review, the advantages of these models are mentioned with emphasis on COVID19. Until now, animal models mostly used to provide crucial clues of many diseases; however, lots of them failed to replicate the human disease condition carefully. Recent advances in tissue engineering and microfabrication represent novel in vitro models of disease, which can simulate the nature of the human diseases in vitro and measure responses to various therapeutic approaches in real-time. Nowadays, engineered models for diseases of the heart, lung, intestine, liver, kidney, cartilage, skin and vascular, endocrine, musculoskeletal, and nervous systems, as well as models of infectious diseases and cancer have been studied. Stem cells mainly induced pluripotent stem cells (iPSCs) can play a significant role in disease modeling and mimic conditions of diseases for individual drug discovery. Stem cells in the form of organoids or 3D-printed constructs can be used to develop in vitro disease models. These models also can play a role to understand the detailed pathophysiology and identify the best drug targets for new appeared disease, COVID19. The models have the potential to reproduce the viral life cycle and the pathology of the illness precisely to find the best option for the treatment of each person individually.

Methods: -

Results: -

Conclusion: In conclusion, in vitro tissue models of diseases such as COVID19 could facilitate understanding the mechanisms of the disease pathology along with choosing the superior treatment approach using drug screening.

Keywords: Disease model, Personalized medicine, COVID19

Interleukin-35 (IL-35) and its Association with Cancer Progression and Poor Prognosis (Review)

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Introduction: Interleukin-35 (IL-35) is a newly identified IL-12 family cytokine. It is mainly produced by Treg and Breg cells and plays an important role in immunosuppression and infection and autoimmune disease prevention. IL-35 is composed of Epstein-Barr-induced protein 3 (EBi3) and IL-12Î± chain (p35) subunits. Its overexpression has been identified in various forms of cancer.

Methods: In the present review study, we searched articles from PubMed, Google Scholar and ScienceDirect with keywords IL-35, cancer, malignancy and tumor. One hundred and sixty-seven articles were found and 132 of them were removed after reading the title or abstract. Review articles were also excluded. Finally, thirty-five articles were selected for this study under the inclusion criteria.

Results: Significant increase Â IL-35 expression in tumor tissue or blood was observed inÂ breast cancer, pancreatic cancer, prostate cancer, leukemia,Â lymphoma, lung cancer,Â nasopharyngeal carcinoma,Â colorectal cancer, gastric cancer, liver cancer, renal cell carcinoma, head and neck cancer,Â laryngeal squamous cell carcinoma and osteosarcoma studies. IL-35 expression levels were higher in plasma and tumor tissue in later stages of cancer or lymphatic metastasis. According to some studies, IL-35 inhibits antitumor T cell responses (mainly Th1 and Th17), protects tumor cells against immune system and promotes tumor development.

Conclusion: IL-35 is linked to cancer progression and tumorigenesis. Regulating its levels might provide a new potential target for cancer prevention, grading or immunotherapy.

Keywords: Cancer, IL-35,Â Tumor,Â Interleukin-35

Investigating the effect of electronic artificial skin on the sense of touch (Review)

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Introduction: Singaporean researchers have developed an electronic artificial skin that can recreate the sense of touch. This device allows people with artificial limbs (such as limbs) to identify objects and even feel sex, temperature and pain. The aim of this study was to investigate the effect of electronic artificial skin on the sense of touch.

Methods: This study was conducted in 2021 by searching for keywords such as artificial skin, electronic skin and tactile sense in valid databases such as: pub med and google scholar, which finally found 15 articles, of which 10 articles 10 the article was used

Results: Based on the studies obtained from the articles, the results show that this device is Asynchronous Coded Electronic Skin (ACES) with a size of 1 square centimeter and has 100 small sensors. Also, the information analysis process of this device is faster than the human nervous system. It is able to identify 20 to 30 different genders and read the braille line with more than 90% accuracy. It is up to the material to be detected. Also, artificial intelligence algorithms have made the device fast detectable.

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: Artificial skin, electronic skin and touch

investigation effect of ethanol on the structure of Kupffer cells in the liver of male pups of rats during pregnancy and lactation (Research Paper)

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Introduction: Alcohol consumed by the mother can pass through the placenta without delay and may affect the fetus immediately and spread rapidly to any body water chamber such as neurons or lipid membranes, and the baby genotype is most likely related to the baby's alcohol consumption. It is after birth. Like other organs, the liver is exposed to intrauterine ethanol. However, little is known about the effect of maternal ethanol exposure on the developing liver. Previous studies have shown that ethanol exposure during pregnancy leads to liver fibrosis and fat degradation by testing abnormal liver function in children with FASD. Blood alcohol concentrations in the fetus are comparable to those in the mother. Alcohol metabolism in pregnant mice increases fetal alcohol and fetal toxicity. Kupffer cells (KCs) are hepatic macrophages that reside in the sinusoids and make up 15% of the hepatocytes and 50% of the macrophages that reside in the body. KC originates in fetal yolk sac precursors and their self-development depends on GM-CSF and M-CSF. Some data suggest that Kupffer cells or their lineage may play a role in erythrocyte maturation during fetal liver hematopoiesis. Have . Deficiency of Kupffer cells in rats after partial hepatectomy (PH) leads to delayed liver regeneration. In the absence of Kupffer cells, there is a decrease in the secretion of TNF-Î± and IL-6 compared to normal liver and the delay in liver regeneration is attributed to the inactivation of NF-ÎºB. During chronic injury, Wnt ligands are released, KC during phagocytosis can lead bipolar ancestors to liver fate. In addition, KCs play an important role in liver regeneration by affecting the aggressive behavior of liver progenitor cells.

Methods: Pregnant rats were randomly divided into 3 experimental groups: the control group receiving distilled water and the oily ethanol group receiving ethanol with oil by gavage up to 28 days after delivery. Mice in the ethanol group received ethanol (4 g / kg) as a solution in

distilled water (40% v / v) as oral gavage from day 0 of gestation until 28 days after delivery. On the 18th day before birth and 28 days after birth, a number of rats were sacrificed for histopathological examination of the liver of the mother and the fetus, and the fetus was examined for weight and appearance. Liver tissue samples were placed at -70 Â° C for biochemical tests. And some other animals under deep anesthesia, then perfusion operation was performed and then the animal's liver was removed. For better fixation, we first changed the liver tissue in 10% paraformaldehyde solution every 12 hours and then histopathological examination was performed.

Results: The study showed that damaged liver cells underwent apoptosis and were phagocytosed by Kupffer and stellar cells, further increasing ROS formation and stellar cell activation.

Conclusion: To repair damaged liver in adults, several highly protected signaling pathways are required for organogenesis to occur during fetal development. Wnt ligands are central secretory glycoproteins for liver repair and are mainly produced by the non-parenchymal cell compartment, especially Kupffer and endothelial cells.

Keywords: Ethanol, liver, Kupffer cells, pregnancy,, rats

investigation Histological and biochemical evaluation of pups and liver of ethanol treated pregnancy mothers in rat (Research Paper)

sajjad kooshki,[1,*] mohammad taghi ghorbanian,[2] iran Goudarzi,[3] hadis kooshki,[4]

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Introduction: In fact, alcohol abuse is a common problem in global health. Excessive alcohol consumption is one of the most effective factors in causing inflammation of the liver (ALD). The effect of alcohol on different tissues depends on the concentration of alcohol in the blood (BAC) depending on how quickly alcohol is absorbed, distributed and metabolized. Continuous alcohol consumption during pregnancy causes serious damage to the developing fetus, the most important consequences of which can be changes in the developing brain and neurobehavioral defects throughout life, as well as leading to a wide range of teratogenic effects. cited. Drinking alcohol, even in moderation, is associated with an increased risk of miscarriage, especially in the first trimester of pregnancy and infertility in women. Ethanol has been shown to be a ligand that induces a death signal to the cell in both in vitro and in vivo conditions, causing programmed death. In animal studies, exposure to alcohol at a stage equivalent to the first trimester of pregnancy in humans caused fetal alcohol syndrome (FAS) and was associated with loss of muscle movement during the second and third trimesters. The third trimester has also been shown to have serious effects on the fetus, as it is associated with a significant increase in essential nutrients in the brain and retina. Frequent consumption of alcohol causes liver dysfunction. Alcohol-induced liver disease is one of the most common causes of liver cancer and cancer mortality, and is also a major cause of leukemia. Ethanol has been shown to cause toxic effects by producing reactive oxygen species (ROS) and inducing lipid peroxidation in various tissues and cells. ROS has been reported to affect the oxidation of proteins, fats. Oxidation damages DNA, inactivating the enzyme and destroying various antioxidant enzymes. These results can cause early stages of liver disease and liver dysfunction. Oxidation of ethanol by the microsomal oxidizing enzyme (cyp2E1) p450 and dihydrogenase causes the accumulation of ROS in the fetal liver.

Ethanol-induced liver pathology is associated with cyp2E1 expression. Excessive expression of cyp2E1 causes fat oxidation and oxidative stress in the fetal liver. The expression level of cyp2E1 in the liver is high because approximately 80% of the ethanol consumed is metabolized in the liver. Ethanol affects MAPKs in cells and systems of different organs, thus showing different pathological effects. Ethanol consumption chronically regulates nitric oxide (NO) levels and the expression level of protein cyclooxygenase (COX) in maternal and neonatal liver tissue. Recent studies by Natabaj have shown that ethanol consumption increases the phosphorylation of jNK, ERK and P38 in the liver of mother and offspring of rat.

Methods: Pregnant rats were randomly divided into 3 experimental groups: the control group receiving distilled water and the oily ethanol group receiving ethanol with oil by gavage up to 28 days after delivery. Mice in the ethanol group received ethanol (4 g / kg) as a solution in distilled water (40% v / v) as oral gavage from day 0 of gestation until 28 days after delivery. On the 18th day before birth and 28 days after birth, a number of rats were sacrificed for histopathological examination of the liver of the mother and the fetus, and the fetus was examined for weight and appearance. Liver tissue samples were placed at -70 Â° C for biochemical tests. And some other animals under deep anesthesia, then perfusion operation was performed and then the animal's liver was removed. For better fixation, we first changed the liver tissue in 10% paraformaldehyde solution every 12 hours and then histopathological examination was performed.

Results: Evaluation of oxidative enzymes showed a significant increase in MDA in the ethanol group compared to the control group ($P < 0.5$). Also, GPX level decreased significantly compared to control ($P < 0.05$). In histopathology, the number of hepatocytes in the ethanol group increased significantly ($P < 0.5$) and caused hepatocyte necrosis and severe weight loss and fetal defect in the ethanol group.

Conclusion: According to the results, ethanol caused severe weight loss and defects before and after birth in the pups as well as damage to hepatocytes, Kupffer cells and maternal liver lobules. The number of Kupffer cells decreased.

Keywords: ethanol, FAS, pups ,pregnancy, rat , liver

Investigation of hsa-miR-136-5p target genes in the main route of tongue cancer by David Analysis (Research Paper)

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Introduction: Tongue cancer is the eighth most prevalent malignancy globally, posing a significant threat to human health. MicroRNAs are a group of small non-coding RNAs that include 21-25 nucleotides. That binding to the sequence in 3â€™UTR of target mRNA. In recent years, miR-136-5p has received much attention as a tumor suppressor for multiple cancers. This study investigated the expression of target genes hsa-miR-136-5P through the comprehensive web-based David method.

Methods: By Considering the role of miR-136-5P in tongue cancer was obtained predicted targets of miR-136-5P with the MIMAT0000250 ID from the MiRBase database and inserted in the MiRwalk2.0 database and received a gene list. Finally, we obtained it in the DAVID database to get the miR-136-5P-related pathways and we got the genes in the main pathway that cause tongue cancer.

Results: The Database for Annotation, Visualization and Integrated Discovery (DAVID, http://david.abcc.ncifcrf.gov/) is an online tool for functional gene classification, which is an essential foundation for high-throughput gene analysis to understand the biological significance of genes. KEGG pathway analyses were conducted using the DAVID online tool; $p<0.05$ was set as the cutoff point. KEGG signaling pathway data and signaling pathway in tongue cancer show as the most statistical pathway associated with hsa-miR-136-5p targeting and it can be said that hsa-miR-136-5p acts as involved in causes tongue cancer.

Conclusion: hsa-miR-136-5p effect in cancer signaling pathway and suppress the ADH1B and ADH1C gene expression and prevents the function of some genes, such as Ras, Mek, Raf, and Sos genes. All in all, we conclude that hsa-miR-136-5p may lead to tongue cancer

Keywords: tongue cancer, hsa-miR-136-5p, MicroRNAs, DAVID database

Investigation of racR gene in thermophilic campylobacter Spp. (Research Paper)

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Introduction: Campylobacter is one of the most common causative agents of bacterial food-borne gastroenteritis in humans worldwide. Thermophilic Campylobacter species like C.jejuni grow between 37Â°C and 42Â°C, (optimally at 41.5Â°C) and are incapable to grow below 30Â°C. The RacR-RacS signal transduction system have a key function in altering gene expression at 42Â°C. The racR gene (reduced ability to colonize), a member of the RacR-RacS system, codes for a regulatory protein that has an effect on the growth of Campylobacter in a temperature-dependent way and on the colonization of the intestinal tract of chickens.

Methods: In all, 136 faecal samples were collected from poultry. The fecal samples were collected using sterile sticks and polyethylene bags (Isun Medical, Tehran, Iran) and transferred to the laboratory of Islamic Azad University, Behbahan branch within one hour of sampling. The samples were subjected for detection of Campylobacter immediately upon arrive to the laboratory. Campylobacter detection in the present study was pre-treatment- apandis Baseri (prÃªt-KB) technique and the medium was blood and antibiotic free Kapandis Baseri (KB) medium (HiMedia, Mumbai, India). To perform the method faecal samples were added (10% (w/v)) in sterile phosphate-buffered saline (0.1 mol l-1, pH 7) (Merck, Germany) to obtained 10% suspension. The suspension was centrifuged at 8500 rpm for 10 min, then it was placed at room temperature. Afterward 10â€“15 min, 0.1 ml supernatant from the tube was plated on the KB medium (HiMedia, Mumbai, India). The plates were incubated at 37Â°C for 48 h in microaerophilic conditions and tested daily for 5 days. All suspected colonies grew on the KB medium confirmed by typical morphology, darting motility, gram staining, oxidase, and catalase tests. The isolates with presumptive Campylobacter character were subjected to standard Campylobacter phenotypic identification tests recommended by Atabay and Corry.These tests included H2S by lead acetate strip, nitrate reduction, growth in 1% glycine and 3.5% NaCl, growth at temperatures 25Â°C, 37Â°C, and 42Â°C, hippurate hydrolysis, indoxyl acetate hydrolysis, urease

production, and resistance to Nalidixic acid (30 Î¼g) and Cephalothin (30 Î¼g). Additional tests for identification of Campylobacters were alkaline phosphatase production, oxidative-fermentative test (OF Test), and glucose fermentation. All items used in the phenotypic identification tests were purchased from Parsalab (Tehran, Iran). At the end, the PCR method was carried out in order to confirm the phenotyping results and detection of racR gene. The PCR assay was done for authentication of Campylobacter and detection of racR gene. DNA was extracted from suspected colony using phenol chloroform method. The PCR was performed in 25 ml of the reaction mixture with a final concentration of 1Ã—PCR reaction mix, 10pgâ€“1Î¼g concentration of template deoxynucleotide triphosphate (DNA), 0.1 â€“1 Âµmol L-1 concentrations of each primer (Macrogen, Inc, Seoul, Korea), 3.2 m mol L-1 MgCl2 solution, and 1.25â€“2.5 U/50 Î¼l of GoTaq DNA polymerase. All items used in the PCR were purchased from Yekta Tajhiz Azma (Tehran, Iran) and the experiment was performed by thermal cycler (Bio-Red, Singapore). A 100-bp DNA ladder (Yekta Tajhiz Azma, Tehran, Iran) was used as a DNA molecular ladder. PCR products were electrophorized using 1% agarose gel (Yekta Tajhiz Azma, Tehran, Iran) at 80 V for 60 minutes. In addition detection of racR gene from each DNA extract was carried out and all amplified DNAs were visualized with UV transilluminator (Heidolph, Germany).

Results: Among 27 Campylobacter strains, including 23 C.jejuni and 4 C.coli, prevalence of racR gene in poultry was 88.89% (24/27) .

Conclusion: The results obtained from present study achieved during March 2020 and May 2020 from 136 samples were collected of which 27 strain of Campylobacter spp. isolated. Of the 27 strains, 23 C.jejuni and 4 C.coli were isolated. This is evidently could concluded that there exist C.jejuni and C.coli in Poultry in behbahan city. The racR gene of Campylobacter spp. Has been reported to be important in the ability to colonize chickens and support optimal growth rates at 42Â°C, suggesting that the racR gene regulates genes important for in vivo colonization in a temperature-dependent manner. In our research, the prevalence rate of racR gene was 88.89%. The results, similar to our research, have been reported where in the prevalence rate of racR gene is high .

Keywords: racR gene, Thermophilic Campylobacters

Investigation of the effect of Enalapril on postoperative abdominal adhesion (Research Paper)

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Introduction: One of the clinical challenges is postoperative adhesions. Renin angiotensin type I receptor antagonists, such as Enalapril, is one of the most important drugs used to treat hypertension and cardiovascular disorders. It reduces TGF-Î² expression. One of the most important pro-fibrotic factors is TGF-Î² cytokine, which involved in the mechanism of increased collagen expression, accumulation of extracellular matrix and consequently fibrosis, and postoperative adhesions are also a result of the fibrosis process. Accordingly, the aim of the present study was to investigate the effect of Enalapril on postoperative adhesions by evaluating histological factors, gene expression and biochemical factors.

Methods: In this experiment, after establishing the adhesion model in the study groups, treatment with Enalapril was performed and after the end of the treatment period and killing the animal, macroscopic examinations of the severity of adhesion carried out using Nair and Leach criteria. The severity of inflammation as well as fibrosis in the adhesive tissues between the cecum and the abdominal wall were evaluated by histopathological examination and H&E and trichrome staining. The expression of collagen 1 and collagen 3 genes was also examined using real time PCR technique. In the continuation of this experiment, the concentration of inflammatory factors IL6, TNF-Î± and fibrotic factor TGF-Î² in the homogeneity of adipose tissues was investigated using ELISA method.

Results: The results of this study showed that treatment with Enalapril reduced the severity of postoperative adhesions. In histological staining studies, the severity of inflammation and fibrosis in the group treated with Enalapril was significantly reduced, and this drug also reduced the fibrotic factor TGF-Î² and the expression of collagen genes.

Conclusion: The results of this experiment showed that Enalapril reduced postoperative adhesions and showed that treatment with this drug reduced the concentration of TGF-Î² and decreased the expression of collagen genes involved in adhesions mechanism so reduced postoperative adhesions. This drug is recommended to prevent postoperative adhesions due to its safety in people who are candidates for surgery.

Keywords: Postoperative adhesions, Enalapril, TGF-Î² fibrotic factor

Involvement of miR-141-3p dysregulation and its targets genes in trastuzumab resistance of HER2-positive breast cancer cells (Research Paper)

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Introduction: One of the most prevalent malignancy in the world is breast cancer which has led to high mortality rate in women. Trastuzumab is one of the most effective drugs for targeted therapy of breast cancer (BC). The response of HER2-positive BC to trastuzumab in early stages is approximately up to 50%. After one year of treatment, several patients show resistance to trastuzumab. In order to increase the therapeutic effectiveness of patients, it is also important to study the molecular mechanisms causing trastuzumab resistance. Studying MicroRNAs (miRNAs) are regarded in cancer prognosis and treatment. Based on the targets, miRNAs can act as either an oncogene or a tumor suppressor. miRNAs dysregulation have been reported in a variety of cancers. Numerous studies have shown that dysregulation of microRNA expression is associated with cancer invasion, metastases, and chemotherapy resistance. According to previous studies, the mechanism of resistance to treatment may be regulated by changing in miRNA expression. Latest experiments have shown that microRNA-141 is concerned in breast tumor cell proliferation and metastases. In current study, we performed the prediction and verification of miR-141-3p target genes including IGF1R and PTEN and the expression of these genes in trastuzumab-resistant cell line compared with sensitive cell line as control sample.

Methods: Cell culture and generation of trastuzumab-resistant cells: BT-474 cells were cultured in supplemented media using a humidified incubator at 37 Â°C. Generation of trastuzumab-resistant cells (BT-474-R) was performed by exposing culture of BT-474 cells to trastuzumab for 6 months. Then, trastuzumab-resistant and sensitive BT-474 cells were

cultured with and without trastuzumab, respectively. Cell survival assay: Cell survival was measured by MTT assay. Cells were seeded in each well of a 96-well plate and incubated for 24 h. Then, trastuzumab was added and incubation continued for 72 h. After removing the medium MTT solution was added and incubated for 4 h at 37 Â°C. After addition of DMSO, agitation was done for 45 min at room temperature and the absorbance values were read at 570 nm. Cell survival was measured by following formula: survival percentage= (absorbance of drug-treated wells â€“ blank wells)/(absorbance of untreated wells â€“ blank wells)Â· 100. IC50 values was calculated by the ED50 Plus v1.0 online software. RNA extraction and quantitative real-time PCR: Total RNA was extracted from BT-474 and BT-474-R cells. The isolated RNA samples were reverse-transcribed into double-stranded cDNA. The samples were subjected to quantitative PCR (qPCR) in the StepOne Real-Time PCR System. GAPDH was used as internal control. Relative abundance of detected transcripts was calculated using the 2âˆ’Î”Î”Ct method. The experiments were performed in triplicate. Prediction of target genes: TargetScan and miRDB were used for prediction of target genes. Related pathway to target genes was predicted Using KEGG pathway analysis.

Results: Trastuzumab-resistant breast cancer cells display survival over parental cells: The parental cells showed a significant reduction in cell proliferation in comparison to resistant cells ($p < 0.01$). At the highest dose of trastuzumab the percentage of cell viability for resistant cells was about 80%, whereas it was about 44% for sensitive cells. The results suggest that trastuzumab-resistant HER2-positive breast cancer cells exhibit proliferation advantages over parental cells. Expression status of the tow selected genes detected by qRT-PCR: Using qRT-PCR the expression level of target genes including IGF1R and PTEN were evaluated in resistant and sensitive BT-474 cells. The expression of both genes were significantly downregulated in BT-474-R cells compare with sensitive cells.

Conclusion: In this study, we found that the development of resistance to trastuzumab may be related to the downregulation of PTEN that is related with AKT/PI3K pathway. The results suggest that downregulation of PTEN induces senescence and consequently secretion of SASP factors. It causes progression and invasion of cancer cells. Increasing the activation of AKT/PI3K pathway as a results of PTEN depletion causes resistant to trastuzumab in BT-474 cell line. Our results emphasize on the importance

to identify proper biomarkers and molecular targets to improve personalized medicine.

Keywords: miR-141-3p, AKT/PI3K pathway, HER2-positive breast cancer, trastuzumab resistance

Isolation and recognization of protease producing bacterium Basillus sp.SM-7 from Caspian sea (Research Paper)

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Introduction: Marine enviroments supply a suitable place for natural microbial communities which in turn serve as a potential origin of pharmaceutical and nutriceutical substance. Proteases are among the most important industerial enzymes Which accounts about 65%from global market for industerial enzymes.

Methods: In this paper,Screening of the protease-producing Bacteria was carried out by skim milk agar.Enzyme assay was investigated by the colorimetric method and the effect of different paramters such as temperature,pH,different NaCl concentration and different ions on enzyme activity were assesed.detection of the isolates was carried out by biochemical and molecular methods

Results: A total of 12 strains with proteolytic activity were isolated among which the strain S-7 with higher clear areola on skim milk agar was choosen for extra analysis. maximum proteolytic activity of the enzyme was observed at 30Â°c,Ph 10.0 ,and the 3% concentration of salinity. Its biochemistery tests and 16s rRNA gene sequencing showed that it is Basillus sp.SM-7.

Conclusion: This resault notifies that protease SM-7 can be used at biotechnology incloding detergent industries,meat processing,â€¦..

Keywords: Key Words: Protease,Caspian sea, proteolytic activity, Isolation,Basillus sp

Isolation of bacteriocin-like inhibitory substances (BLISs)-producing Staphylococcus epidermidis from different Iranian clinical sources (Research Paper)

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Introduction: The emergence of pan-drug resistant strains (PDR) of bacteria has led to renewed efforts to identify alternative agents, such as bacteriocins and bacteriocin-like inhibitory substances (BLISs). In recent years, Bacteriocins have been recognized as natural preservatives in food and drug industries, also, nowadays, they are used as substitutes of chemical antibiotics for treatment of infections.

Methods: In a cross-sectional study, 150 Staphylococcus epidermidis strains were isolated from different Iranian clinical sources (patients with burns, wound and skin infections, UTI, diarrhea, eye infections, human skin wounds, and soft tissue infections) during a 3-month period. isolates were investigated by Spot test and Well diffusion test for their ability to produce compounds exhibiting antibacterial activity. BLISs production was induced by mitomycin C (2 g/mL) in S. epidermidis.

Results: 23 isolated from the S. epidermidis had potent activity against Bacillus cereus, Listeria monocytogenes, Klebsiella spp., Staphylococcus aureus, P. aeruginosa, Proteus spp. and Vibrio parahaemolyticus. The BLIS was heat-stable (up to 100Â°C for 15 min) and active within a pH range of 3 - 9. High yields of pyocin at 35 â€“ 37Â°C, which declined sharply at temperatures above 37Â°C were obtained from all the producing strains. BLIS production started in the mid-exponential phase of growth, and the maximum level occurred in the late-stationary phase after 30 hours of incubation at 37Â°C.

Conclusion: The produced bacteriocin had a wide antibacterial activity spectrum against the gram-positive and negative bacteria, in particular pathogenic bacteria, also was resistant against heat and pH ranges. As a result, use of bacteriocin in food and drug industry, as animal feed, and as a substitute for chemical antibiotics is recommended.

Keywords: Bacteriocin, Staphylococcus epidermidis, Antibacterial, Drug-resistant

Lake Urmia halophiles are valuable microorganisms in the production of biotechnological products (Review)

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Introduction: In recent years, the links between human life and biotechnology have encouraged researchers to find more efficient microorganisms in the production of pharmaceuticals and other necessary materials. Study of halophytic microorganisms has gained importance due to their potentialities in biotechnology. Consequently, Lake Urmia, as Iranâ€™s largest endorheic salt-lake and one of the hyper-saline lakes in the world that is similar to the Great Salt Lake in the United States, enjoys great importance as a suitable substrate for development and extraction of these microorganisms.

Methods: By studying the research that has been done in the field of identifying the biological factors of this lake, a number of founded species were examined.

Results: Studies for determining the biosphere reserves in this lake have identified various groups of halophilic microorganisms including the bacterial genus Salinivibrio strains of which are used to produce the enzyme L-asparaginase, an effective drug for treating acute lymphoblastic leukemia.

Conclusion: Utilization of this resource can be effective in supplying the biotechnological products needed in the country. In addition, export of these products to the global market will earn foreign currency besides improving Iranâ€™s scientific status in the world. Therefore, in order to achieve these objectives, it is necessary to pay greater attention to Lake Urmia and the other valuable biosphere reserves in the country.

Keywords: Lake Urmia - Halophilic microorganisms -Biotechnological products

Melatonin and its effects on coronavirus (Review)

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Introduction: Melatonin is a hormone that is released by the pineal gland in the brain and helps regulate the body's sleep-wake cycle. In addition to its role as a sleep cycle regulator, melatonin is a powerful antioxidant and cleanser of free radicals and also causes an impact on the function of several important antioxidant enzymes such as superoxide dismuta, glutathione peroxidase, glutathione reductase and catalase. It plays melatonin as a wonderful antioxidant. Some symptoms, such as excessive inflammation and increased immune system reaction, can be symptoms of coronavirs. This condition leads to cytokine storms and subsequent progression to acute lung injury/acute respiratory syndrome and often death. Studies have shown that melatonin protects the body against acute respiratory syndrome caused by viruses and other pathogens, which is one of the effects of melatonin on inflammation.

Methods: Melatonin properties help us to be more resistant to stressful conditions and deal with viral diseases easily. This hormone makes the body's strong molecules safer against the passage of time and less aging and complications. When our immune system is stronger, we deal well with diseases. Studies have shown that melatonin protects the body against acute respiratory syndrome caused by viruses and other pathogens due to the effects of melatonin on inflammation. Melatonin may have two completely different types of effects in Covid-19, each depending on the dosage and severity of the disease. The Effect of Melatonin and NLRP3 Receptor 3 (NLRP3(NOD) is considered as part of the immune system. Viral pathogens to strengthen inflammation activate NLRP3. Melatonin by inhibiting this receptor affects the reduction of lung damage and inflammation of the airways, in these cases, melatonin reduces the penetration of macrophages and neutrophils into the damaged lung by inhibiting NLRP3 inflammation. In studies conducted on mice, inhibition of NLRP3 in the early stage of infection increases mortality. While suppression of NLRP3 at the height of infection causes a protective effect. This review may show that high-dose melatonin is best used in the acute lung stage. The stage is ARDS. That is, when the inflammation becomes

more intense. Effect of Melatonin and ACE2 In addition to being a potent antioxidant, melatonin can have direct antiviral effects against COVID-19. In healthy people, melatonin levels decrease after the age of 40. Decreased levels of antioxidants and melatonin after the age of 40 can explain the cause of high mortality in patients with COVID-19. Melatonin indirectly affects ace2 function. ACE2 is an important receptor in the incidence of viral coronavirus infection.

Results: Melatonin may play an important role in the prevention and treatment of covid-19. The effect of melatonin even seems to depend on its dosage: Taking low doses (6-3 mg/day) of melatonin is useful for prevention or treatment in the early stages of corona disease. Taking higher doses (20-40 mg per day) of melatonin is useful for managing lung damage or ARDS. Melatonin can also have indirect benefits in managing intensive care patients by reducing vascular permeability, anxiety, sedation and improving sleep quality, all of which may be beneficial for better clinical outcomes for COVID-19 patients.

Conclusion: Studies conducted by Columbia University researchers show that patients with corona who need intubation and mechanical ventilation due to respiratory distress can benefit from melatonin hormone therapy, in addition, exposure to melatonin following intubation has also been associated with a positive survival result among patients with COVID-19 who need mechanical ventilation. However, no advantages have been observed in other non-coronavirus patients who need mechanical ventilation. This suggests that melatonin may, in the most severe cases of COVID-19, target inflammation caused by acute respiratory syndrome, coronavirus 2 (SARS-CoV-2). Following infection with SARS-CoV-2 most people usually experience symptoms such as fever, cough, fatigue, shortness of breath and loss of taste or smell. However, there are also some rare symptoms of corona. The most severe symptom of this disease is respiratory hayd syndrome, which in the worst case scenario, the patient may need intubation, mechanical ventilation and even potentially a lung pyodeon. Among the candida therapies that researchers have examined for the treatment of COVID-19, hormonal drugs such as dexamethasone have shown promising results.

Keywords: COVID-19, melatonin hormones, immune system, inflammation

Microalgae: Therapeutic Potentials and Applications (Review)

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Introduction: Microalgae are photosynthetic microorganisms. They are classified into two categories prokaryotes and eukaryotes. They can live in many different environments. these microorganisms are capable of producing different types of bioactive molecules such as carotenoids, polysaccharides, vitamins, lipids with their potential uses as antioxidant, anti-inflammatory, antitumor, anticancer, antimicrobial, antiviral, and anti-allergic agents; so they have very important applications in the biomedical and pharmaceutical industry. furthermore, microalgae have applications in cosmetic products, environmental biotechnology, animal feed. This study aims to review the therapeutic potentials and applications of microalgae in drug delivery and cosmetics.

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: Microalgae, specifically Chlamydomonas reinhardtii, are suitable to use as vaccine transporter because they are safe and contain a single chloroplast that expressed proteins with high accumulation there. E7 oncoprotein for HPV vaccine is an example of these recombinant proteins. Nowadays, most monoclonal antibodies are producing in the Chinese hamster ovary(CHO); also of high cost, there is the possibility of contamination with human pathogens. Microalgae have some benefits that can be used as alternative host cells. They are better than bacterial

cells for post-translational modifications (PTMs) on human recombinant proteins and due to their high growth rate, convenient handling and simple culturing are superior to other eukaryotic hosts. Several microalgae extracts have antiviral, antibacterial, antifungal, and antiprotozoal activities such as indoles, phenols, fatty acids, and volatile halogenated hydrocarbons. A monogalactosyl diacylglyceride (MGDG) extracted from Coccomyxa sp. Cause some physical changes in HPV to envelop so this virus could not attach to host cell so MGDG has an antiviral effect. Today, antibiotic resistance is an important challenge in the treatment of infectious diseases. As a result, searching for novel antibiotics is necessary. A mixture of fatty acids from Chlorella has inhibitory activity against bacteria. In addition, microalgae compounds showed antibiofilm activity which is important in infectious diseases. For example, extracts of two microalgae, C. vulgaris, and D. salina can inhibit biofilm formation and prevent Dental caries. Some carbohydrates, lipids, and phycobiliproteins extracted from microalgae have shown antiproliferative and apoptotic effects in different cancers. Fucoidan is a sulfated polysaccharide extracted from different microalgae such as Fucus vesicles, which inhibit angiogenesis and metastasis by downregulating kinase activity and activation of caspase 3/7 in the human lymphoma cell line, melanoma, human colon cancer, breast cancer, lung carcinoma, and human promyeloid leukemia. Furthermore, Phycocyanin is a Phycobiliprotein extracted from some microalgae such as spirulina platensis which inhibit the growth of human hepatocellular carcinoma, lung, colon, and human leukemia cells. Microalgae and COVID-19 treatment Today coronavirus disease (COVID-19) is the most important health issue all over the world and there is an urgent need for finding effective treatments for this disease and preventing the death of hundreds of thousands of people. Researches indicate Acute Respiratory Distress Syndrome (ARDS) as a result of Cytokine Strom Syndrome (CSS) is one of the main causes of death in a patient with COVID-19. In CSS the immune system becomes hyperactive and causes acute lung injury (ALI). So natural compounds with anti-inflammatory and immunomodulatory could help them. Astaxanthin is a carotenoid with anti-inflammatory, immunomodulatory, anti-oxidative, and some other therapeutic potential. Haematococcus pluvalis is a microalga that is the origin of natural astaxanthin. Studies show the use of this carotenoid in COVID-19 patients can alleviate cytokine storms and prevent ARDS and ALI. Carrageenan is a sulfated polysaccharide with the origin of microalgae that can inhibit virus attachment, transcription, and replication of the virus in the host cell. Phycocyanin, a pigment from

spirulina is an inhibitor of NADPH oxidase and has Anti-inflammatory activity. It seems microalgae specifically spirulina is a good candidate for adjuvant therapy of COVID-19 patients.

Conclusion: Understanding the aspects of the biological features of the microalgae will help us to develop Drug and gene delivery systems.

Keywords: Microalgae, Therapeutic effect, COVID-19, Drug delivery

Molecular docking analysis of PSA-specific aptamers: An in Silico Approach (Research Paper)

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Introduction: One of the most important pieces of information in the forensic is the diagnosis of semen in sexual assaults. Prostate-specific antigen (PSA) is one of the most specific components for semen, so finds a reliable method for identification of semen based on PSA in forensic investigations is a necessity. Although the use of antibody known as a reliable component for biosensors, but antibody production requires complex laboratory equipment and methods, so the process of antibody production and purification is time-consuming and expensive. Aptamers (a group of single-stranded nucleic acids of DNA or RNA) compared to monoclonal antibodies because of their affinity and specificity. The purpose of this computational study is to evaluate the docking process of PSA and its specific Aptamers by a range of bioinformatics tools.

Methods: In this study, we retrieved the sequence of specific aptamers from a previous study and predicted the secondary structure of each aptamer by RNAfold server. Next, the third structure of each aptamer was designed by 3dRNA server, and the energy of each aptamer minimized by GROMACS tool based on Amber Force-Field. Next, the refinement of each aptamer structure was performed by QRNAS software. Finally, the docking analysis was accomplished by PatchDock and FiberDock tools.

Results: The purpose of this study was docking analysis of each aptamer and PSA, for this purpose, the predicted structures of each aptamer

reached the most stable form, and a simulation run by the GROMACS tool according to the Amber force-field. Next, to refinement the predicted structure of each aptamer, the QRNAS proprietary tool was used. the refined structures of each aptamer used to perform rigid and flexible docking. According to the results of the rigid docking, VI and XIII aptamers get the highest score by rigid docking on the PatchDock server in comparison to the other aptamers. Finally, to identify the most correct transform obtained by rigid docking for each aptamer, we performed Flexible docking. According to the results of this computational study, VI and XIII aptamers seem to be more suitable than other aptamers for PSA detection.

Conclusion: The results of this study showed that the wide range of accessible bioinformatics tools can be used before wet laboratory analysis in order to design a laboratory and scientific study more wisely and preserve cost and money before running the laboratory analysis. According to the results of this study, we determined the most suitable aptamers for PSA detection and provided valuable information to go-ahead and run laboratory analysis.

Keywords: molecular docking simulation, aptamer, bioinformatics, computational biology.

Naloxone in the formulation of inactivated COVID-19 vaccine candidate improved cellular and humoral immune responses (Research Paper)

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Introduction: COVID-19 is a novel coronavirus from the same family of SARS-COVID-2 that has presented a major threat to public health worldwide. The major sources of the disease that is spread through respiratory droplets and direct contact are currently wild animal hosts and infected patients. The global spread of SARS-CoV-2 has led to an urgent attempt to develop a vaccine. The potency of a vaccine is highly depends on the nature of adjuvant. Opioids are immune modulating agents that improve the immune responses against vaccines. Naloxone (NLX) is an opioid receptor antagonist approved by the FDA and administered to people with opioid peptide-induced respiratory toxicity. Various studies demonstrated that NLX can be used as an adjuvant for designing microbial vaccines. In this study, inactivated COVID-19 virus formulated in Alum and NLX and then immune responses versus the vaccines were assessed in the experimental mice.

Methods: A SARS-CoV-2 strain was isolated from pharyngeal sample of a patient and cultivated in Vero cell line for mass production. The virus was inactivated with formalin and after purification quantified with Bradford. Then 4Âµg of inactivated COVID-19 virus in PBS buffer was mixed with 200Âµg of Alum hydroxide adjuvant and shaked at 100RPM and allowed that the viral particles to adsorb on the surface of Alum gel. One dose of Alum-formulated vaccine was admixed with 200 Âµg of NLX (10 mg/kg) as inactivated COVID-19 Alum-NLX10 vaccine and one dose of Alum-formulated vaccine was admixed with 60 Âµg of NLX (3 mg/kg) as inactivated COVID-19 Alum-NLX3 vaccine. In addition, inactivated COVID-

19 virus was admixed with Freund adjuvant (50/50) and homogenized using homogenizer to develop a homogen suspension. Six-to eight-week-old male BALB/c mice (N=50) were purchased from Royan Institute of Iran and assigned into 5 experimental groups (N=10) as below; Group 1: Inactivated COVID-19-Alum vaccine. Group 2: Inactivated COVID-19-Alum+ NLX 3mg/kg vaccine. Group 3: Inactivated COVID-19- Alum+ NLX 10mg/kg vaccine. Group 4: Inactivated COVID-19- Freund adjuvant vaccine. Group 5: Mice were immunized with PBS as control group. Experimental mice were immunized subcutaneously with 4Âµg of vaccine, two times on days 0 and 14 and two weeks after the final immunization, immunologic parameters were assessed.

Results: Immunization with COVID-19-Alum-NLX10 shows a significant increase of IFN-Î³ cytokine versus COVID-19-Alum, COVID-19-Alum-NLX3 and control groups (P< 0.0033). Immunization with COVID-19-Alum-NLX3 shows a significant decrease of IL-4 cytokine versus COVID-19-Alum group (P< 0.0133). The results of CTL activity based on Gr-B secretion showed that immunization with COVID-19-Alum-NLX10 resulted to a significant increase versus COVID-19-Alum and control groups (P<0.0011). Results of specific IgG titer in the experimental groups showed that immunization with COVID-19-Alum-NLX3, COVID-19-Alum-NLX10 and COVID-19-Freund resulted to an increase of IgG titer versus COVID-19-Alum and control groups. Results of specific IgG1 and IgG2a response showed that all formulations of COVID-19 vaccine induced both of these isotypes.

Conclusion: It seems that Naloxone in the vaccine formulation of COVID-19 vaccine improved cellular and humoral immune responses in parallel to previous studies on the other microbial vaccines. The results of the present study are encouraging to pursue the study in a clinical trial of human.

Keywords: Inactivated COVID-19, Alum, Naloxone, Vaccine formulation, Adjuvant.

Nanobiotechnology and application of the surface layer of bacteria for the preparation of anti-cancer vaccines (Review)

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Introduction: When cancer cell antigens are injected into the body, it does not elicit an immune response, but if combined with the surface layer, it induces a T cell response, NK cells and macrophages and the removal of cancer cells. Simon and colleagues chemically attached carcinogenic glycans such as T-glycans and Lewisy antigen to the surface layer, which retains its cumulative properties and induces strong immune responses. The goal is to use the surface layer of bacteria to make a cancer vaccine.

Methods: In this study, a review of new articles in scientific databases was searched and finally used to organize the article.

Results: Most of the surface layer of bacteria such as Bacillus stearothermophilus Clostridium; Thermohydrosulfuricum and Bacillus aloe. Lactobacillus brevis is one of the most important candidates for anti-cancer vaccine, which is of special importance due to its probiotic properties and ability to grow at acidic pH and resistance to biliary bile salts. It is used as a C_myk adjuvant, which is a proto-oncogene. The surface layer of this bacterium is also used to treat viral infections.

Conclusion: The surface layer has potential applications for making epitope carriers for use in certain vaccines, especially the bacterium Caulobacter crescentus is a bacterium of the environment and nature and is not pathogenic and the protein expression system is very stable and the surface layer protein secretion is high and it can be used for mass production of recombinant protein.

Keywords: Nanobiotechnology; Applied; Surface layer; bacteria ; vaccine ; Anticancer

Neuromuscular blockers, Pharmaceutical Biotechnology solution for terminate to ARDS arising from Covid-19 (Research Paper)

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Introduction: With the ungovernable spread covid-19, humans after failure in controlling of proliferation process, sought to reduce the number of deaths caused by virus. Inflammation of lung tissue and make Acute respiratory distress syndrome (ARDS) and reduce SPO2 is the main cause of death of Coronavirus patients, if a person can tolerate ARDS while having coronavirus, probability of survival is greatly increased.

Methods: The method of this research is based on case reports files as well as books and articles on virology and clinical pharmacy.

Results: Neuromuscular blockers are based on acetylcholine receptors and are made using in vitro pharmaceutical biotechnology. The results of this study show that the use of Neuromuscular blockers in Coronavirus patients causes a feeling of relaxation, prevention of stress and anxiety caused by the progression of the disease. One of the problems of patients with Coronavirus disease is the significant activity of the immune system to fight the virus, increased secretion of lymphocytes in the body and thus increased inflammation in various tissues of the body, This increase inflammation in people with underlying hypertension or diabetes can increase the risk of ischemia in vital organs, such as heart and brain, Neuromuscular blockers reduce heart rate by acting on myocardial cells, thereby reducing the risk of stroke in patients with Coronavirus disease. The main use of Neuromuscular blockers in this context is to increase tolerance in a person with ARDS. Neuromuscular blockers reduce activity in the intercostal muscles and diaphragm, as a result, if a person with Coronavirus disease suffers from ARDS, it can breathe with less pain and more easily withstand the pressure of a mechanical ventilator, resulting in more days to live and Make recovery process be easier.

Conclusion: Early administration of Neuromuscular blockers means that the patient with Coronavirus will not need to go to artificial sleep for use the mechanical ventilator, will breathes with less pain and healing process is faster.

Keywords: Neuromuscular blockers, Coronavirus, ARDS, Pain

Numerical study on the transport phenomena for microalgae cultivation in a foam bed photobioreactor (Research Paper)

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Introduction: Microalgae are an engaged green feed for bulk materials, like the chemicals, energy or feed constituents. For decreasing the production costs of microalgal biomass, a modern bubble column photobioreactor has been created that this plan is based on the usage of liquid foams as a growth bed in order to microalgal cells. Liquid foam bed photobioreactors (LFB-PBR) have various benefits over common. This advantages including: Increase contacting time between liquid /gas phases the great gas holdup of liquid foams caused on decreasing light efficacy path. Due to this little irradiance path, high cell density will be gained, which results in the decrease of biomass separation and purification. High interphase surface presented via liquid foams, improves the mass transfer rates. Enhancing mass transfer rates and the little hydrostatic pressure in the bioreactor caused a reduction in energy needs. Furthermore, in LFB-PBR, CO2 biofixation yield may be achieved because of the high residence time of the CO2 phase in the column. The low pressure depletion in LFB-PBR also caused to reduction construction requirements. So, this research focused on the simulation of a liquid foam bed photobioreactor (LFB-PBR) using computational fluid dynamics (CFD) to obtain the maximum possible high-density culture (HDC). It is worthy to note that mixture method is applied as the multiphase model and COMSOL Multiphysics 5.5Â® was used.

Methods: In CFD simulation the basic equations included continuity equation, momentum balance and species reaction equations are mathematically presented. In addition, in this research, a model for characterizing light transfer is presented. All equations were computed in Comsol multiphysics software 5.5 (64bit), which calculated partial differential equations through finite element method (FEM). Coupling of hydrodynamic and mass transport was applied, and then another one way coupling from concentration field to radiative model was used. Suitable algae species chlorella sorokiniana and chlorella vulgaris were selected. The light attenuation in LFB-PBR was modelled with Lambert-Beer law. CFD

simulations were carried out on a 24-logical super processor system and 96 GB of random access memory. Three-dimensional hexahedral meshes of the LFB-PBR were created and the grid-dependency test was checked, and finally the grid of 10504 elements with 0.28 mm size was used for all the simulations

Results: The accuracy of CFD simulations was verified by comparing with experimental data reported by Agnes Janoska (2018, Dissertation in Wageningen university). Concentration profiles of algae biomass, gasses species (oxygen and carbon dioxide), as well as velocity of dispersed and continues phases were compared with experimental results. Furthermore, light scattering profile versus total time of a batch system of LFB-PBR was obtained. It can be seen that the CFD predictions are matching the experimental data within 80%. According to the obtained results, in the downward of column carbon dioxide is consumed and oxygen is released. Increasing of radial profiles related to the oxygen concentration and algal biomass inside the reactor was observed, while concentration of carbon dioxide was decreased, these finding are in accordance with photosynthetic reaction. Hence, in the layer close to the glass wall, the reaction conversion efficiency was the highest and the main reason for these changes is related to the photoinhibition phenomenon in the microalgae cultivation process. Ccomputational results also show values of dispersed phase volume fraction (liquid phase) swiftly decreases along the height of photobioreactor and in Z=20cm reduction percentage is more than 90%, additionally biomass density is reached to 30 g/L while light intensity was about 1500 Î¼mol m-2 s-1.

Conclusion: Prediction of gas holdup and dispersed phase volume fraction (liquid phase) is of great importance in determining liquid circulation, mixing, mass and light transfer in LFB-PBR and it is of critical importance in photobioreactors design, besides; recirculation rate are basic operational factors for the foam bed photobioreactor, determining its yield and energy requirements. In conclusion, LFB-PBR is an engaged bioprocess for microalgae biomass production.

Keywords: CFD, Microalgae, Photobioreactor, LFB-PBR, Transport equations

Optimization of loop mediated idothermal amplification (LAMP) assay for the detection of Leishmania DNA in Blood samples (Research Paper)

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Introduction: A large group of diseases caused by Leishmania speciesare called leishmaniasis. Leishmania is a protozoan parasite and belongs to the trypanozomatidae family(Gualda et al., 2015). The development of skin-mucosal, cutaneous or visceral disease depends on the immune response of the host and specific species of Leishmania(Andreadou et al., 2014). In 89 countries, Leishmaniasis is recognized as an endemic disease and more than 350 million people are affected(Mohammadiha et al., 2013). Half a million cases are added annually and 50000 cases have died. Leishmania parasites are transmitted to humans by infected mosquito bites (Phlebotomine sandfly)(Gao et al., 2015). Leishmania infantum or Chagasi causes Visceral Leishmaniasis (VL) and Kala-azar and is often fatal(Verma et al., 2013). VL is a zoonotic and endemic disease in northwest and southern Iran(Verma et al., 2013). VL could be fatal if not treated. Therefore, it is important to diagnose this disease accurately. The disease has symptoms similar to other diseases and makes diagnosis more difficult and complex. VL is the second cause of tropical diseases and the average death rate is 20000 to 40000 deaths annually(Yurchenko et al., 1999; da Silva et al., 2013). The definitive diagnosis of Leishmaniasis is based on clinical, epidemiological, and laboratory tests. Common methods are serologic and parasitology test and these make it possible to diagnose Leishmaniasis reliably. Parasitological studies showed that Leishmania infantum presents in liver, spleen aspiration, lymph nodes, and bone marrow. Many patients are not properly diagnosed because the sensitivity of the microscopic studies is low(da Silva et al., 2013). In general, serologic methods are not valuable to evaluate treatment because the results remain positive for months or years after clinical treatment and they may not be good criteria for infection diagnosis. These tests cannot be used in relapses because the antibodies remain after treatment for a long time, many people have high antibody titers against the disease in endemic areas because they contact with these species for a long time and have asymptomatic infections(Poon et al., 2006). In addition, serologic tests such as indirect immunofluorescence assay (IFA), Enzyme-linked immunosorbent assay (ELISA), have false negative results and cross-react

with other diseases(Poon et al., 2006). Direct examination is inexpensive and easy, but when the number of parasites is low in the tissue, these tests lack sensitivity and require high skill. Also parasites culture takes a long time and requires special conditions(Poon et al., 2006). PCR methods are better than old methods and are highly sensitive and have less invasive sampling because peripheral blood specimens can be used. The sensitivity of PCR methods is different and depends on the target sequence and the most common target gene sequences are ITS1 and Kinetoplast minicircle genes (kDNA)(Gao et al., 2015). Real-time PCR is a molecular method. Compared with common PCR, it has high sensitivity of detection especially for blood specimens. In addition, the test time is short because electrophoresis is not required. However, Real-time PCR has limitations such as high cost, the need for special equipment, skillful people and a system for diagnosis and analysis(da Silva et al., 2013). Firstly LAMP was introduced by Notomie in 2000. This method has a high sensitivity and rapidity for DNA replication at a constant temperature (60-65 ÂºC)(Yurchenko et al., 1999). Abbasi et al. (2013) evaluated the performance of LAMP to detect low concentrations of Leishmania DNA in biological specimens and the results showed that LAMP and Real-time PCR had high sensitivity and the detection limit was 1 fg of the target DNA in each reaction(Abbasi et al., 2013). In addition, Chun-hua Gao et al. (2015) showed that the detection limit of LAMP was 1 fg of Leishmania infantum DNA in Canine VL sample(Gao et al., 2015). The LAMP technique is more sensitive than other assays such as PCR, ELISA, and microscopic methods for detection of Leishmania in dogs(Hamburger et al., 2013). Some researchers observed that the LAMP causes the mixture of reaction to become turbid (which shows DNA replication) and does not require electrophoresis. Also, it is more sensitive than PCR for detection(Yurchenko et al., 1999). For VL diagnosis, the gold standard is mainly the detection of parasites in splenic aspiration culture, but it causes bleeding and requires surgery(Koltas et al., 2016; Toubanaki et al., 2016). Overall, there is no acceptable gold standard for the Leishmaniasis diagnosis, so far(Koltas et al., 2016). According to the problems for the Leishmaniasis diagnosis in other molecular methods, we designed the experiment to increase the rapidity, accuracy, specificity, and convenience of the test. The LAMP can replicate small copies of DNA (109 molecules) in isothermal conditions for one hour. In this study, we designed a set of primers for LAMP DNA amplification appropriate for the detection of Leishmania infantum, major, and tropica using ITS2 as region. The sensitivity and specificity of LAMP assay were tested by clinical samples.

Methods: Ethical concerns Study procedures were approved by the ethical committee at Fasa University of Medical Sciences, and the ethical code is IR.FUMS.REC.1395.130. Sample Genomic DNA was obtained from the following Leishmania reference strains: L.major (MHOM/IR/75/ER), L. infantum (MCAN/IR/97/LON490), L. tropica (MHOM/SU/74/K27). These were provided by the parasitology department of Shiraz University of Medical Sciences. DNA Extraction The Leishmania was cultured in RPMI 1640 medium (which contained 10 to 15% fetal bovine serum (FBS), penicillin and streptomycin antibiotics). After the number of parasites reached one million per ml, DNA was extracted by yekta tajhiz azma (YTA) kit with cat No: YT 9030 according to the following steps: First, 200 Âµl of the TG1 buffer was mixed with the sample by pipetting and 20 Âµl Proteinase K was added to the sample and these were mixed by vortex. The mixture was incubated at 60 ÂºC for one hour and was mixed every 10 to 15 minutes by vortex and the lysis process was completed. Then TG2 buffer (200Âµl) was added and mixed and incubated at 70 ÂºC for 10 minutes and ethanol (200Âµl) was added and these combinations were mixed by vortex. The column was placed in a new collection tube and washed with water buffer (500Âµ1) and centrifuged at 1400 rpm for one minute, and the bottom solution was discarded. The column was washed with water buffer (850Âµl) and centrifuged at 1400 rpm for 1 minute then tube bottom solution was discarded, and centrifuged at 1400 rpm for three minutes to dry the column completely. The column was placed in the elution tube and the elution buffer (50 Âµl) was added to the column center and remained in the same position for three minutes. In addition, the centrifuge was carried out at 1400 rpm for 2 minutes, and the extracted DNA was stored at â€“ 20 ÂºC. LAMP Primer Design The LAMP primer sets (external primers: F3 and B3, internal primers: FIP and BIP) were designed using Primer Explorer software (http://primerexplorer.jp/e/) based on shared ITS2 DNA sequences of L. infantum, major, and tropica (Table 1). The locations of the targeted sequences are shown within the conserved Leishmania ITS2 region in Fig.1. Table1. Nucleotide sequences of LAMP primers designed for detection of L.major (MHOM/IR/75/ER), L. infantum (MCAN/IR/97/LON490), L. tropica (MHOM/SU/74/K27) ITS2 region. Sequence PRIMER TM Region ACCAAAACGAGAATTCAACTT F3 52.01 ITS2 TCTTTTTTCTCTGTGCGTAC B3 53.20 TACCACACAGAGAGAGAGCCACCGTTGGCCATTTTTTGCT FIP 73.55 TAGAAGTAGGTTGTGTGTGTGTATGTATGAGAGAGTGAGGGCG BIP 73.25 Fig1. DNA sequences of the 3 species of Leishmania ITS2 region showing the location of the LAMP primers on the sequences shared by different

Leishmania species. LAMP assays The total volume of LAMP reaction mixture was 25 Âµl that contain 2.5 Âµl enzyme reaction buffer (New England Biolabs inc., MA, USA), 40 pmoles FIP and BIP, 5 pmoles F3 and B3 external primers, 8 units of Bst polymerase (New England Biolabs inc., MA, USA), 1.4 mM dNTP mixture; 0.8 M Betaine and DNA template 1 Âµl. The LAMP reaction mixture carried out at 60 ÂºC for 2 hours in water bath. The color of specimens changed by the addition of SYBR Green I in the micro-tubes. Conventional PCR, Real-time PCR, Nested PCR To compare the molecular techniques a conventional PCR, Real-time PCR, Nested PCR for detection of L.infantum DNA was performed. Primers were designed by GENE Runner software, cheeked by primer3 online software of NCBI (Table 2). . Table2. A: The sequences of PCR primers for Leishmania infantum; B: The sequences of PCR primers for Leishmania major, Leishmania tropica; C: Nested PCR (intra primers); D: Nested PCR (extra primers); E: The sequences of Real Time PCR primer sequence. Product size(bp) Sequence Primer TM Region 977 CATTTTCCGATGATTACACCCAA Forward 53.76 18S ITS1, 5.8S, ITS2 TCTTTTTTCTCTGTGCGTAC Reverse 53.2 1059 CATTTTCCGATGATTACACCCAA Forward 53.76 18S ITS1, 5.8S, ITS2 AAGTTCGGCGGGTAGTC Reverse 55.18 189 AACTCCTCTCTGGTGCTTGC Forward 59.35 ITS2, (IN) AAAATGGCCAACGCGAAGTT Reverse 55.25 439 AGGCGTGTGTTTGTGTTGTG Forward 57.3 ITS1, 5.8S, ITS2 (EXT) AGAGTGAGGGCGCGGATA Reverse 58.24 137 AGGCGTGTGTTTGTGTTGTG Forward 57.3 ITS2 GCAAGCACCAGAGAGGAGTT Backward 59.3 Specificity and Sensitivity of LAMP Reaction a) Specificity Toxoplasma gondii, Trypanosoma cruzi, Cryptosporidium parvum, and Escherichia coli DNA samples were used as negative control sample to evaluate the specificity of the LAMP assay. b)Sensitivity LAMP reaction conditions were tested on serial dilutions of plasmid HPV DNA to confirm minimum copy number detection thresholds. For this purpose After PCR of this region the sequencing was confirmed whit sequencing and the fragments were prepared for cloning. E.coli TOP10 was used as host and pTZ57R/T plasmid as vector and the thermo scientific, TA-cloning kit, Cat No. K1214 was used at some stages. The concentrations of extracted plasmid of all three Leishmania strains were measured by spectrophotometer. LAMP was carried out to evaluate sensitivity on Ten-fold serial dilutions (nâ€‰=â€‰9) of the concentrations of extracted plasmid were prepared in PBS Buffer resulting in a range from 34.2ng to 34.2fg/Âµl (Fig2). Fig 2. Serial dilution of Plasmid that cloned with 18s, ITS1, 5.8s and ITS2 region Clinical samples: The sensitivity and specificity of LAMP assay for detection of VL were analyzed in clinical samples blood from human, and five

samples obtained from dog. The samples were placed in eppendorf and stored at -20 ÂºC for later DNA extraction. 10 of 15 clinical samples were obtained from human were confirmed by PCR and ELISA (enzyme-linked immunosorbent assay). Clinical signs for approval VL were also confirmed by a specialist at the Valfajr Moolecular Center and 5 peripheral blood samples that obtain from dog were confirmed by Shiraz Parasitology Department.

Results: Specificity and Sensitivity of LAMP assay for detection leishmania The results was shown all of negative controls (Toxoplasma gondii, Trypanosoma cruzi, Cryptosporidium parvum, and Escherichia coli) samples were negative. The sensitivity of the LAMP assay for Leishmania infantum, major, and tropica strains was 400, 4Ã—107, 4Ã—107 copy number of plasmid DNA, respectively (Fig 3). The results showed that these primers detected 4 Ã— 102 Leishmania infantum plasmids in the LAMP method and each parasite had about 200 ITS2, so this method can detect about 2 parasites per 1Âµl. Fig3. A: The LAMP assay on Leishmania infantum plasmid serial dilutions which was showed that eight tube was positive and other tubes and negative control tube were negative. B: The LAMP assay on Leishmania major plasmid serial dilutions which was showed that third tube was positive and other tubes and negative control tube were negative. C: The LAMP test on the third colony of plasmids for Leishmania tropica which was showed that first to fourth tubes were positive and the negative control tube was negative. LAMP assay was carried out on clinical specimens and the results showed that 12 of 15 specimens were positive, so its sensitivity was 80% (Fig 4). Fig4: The color of specimens changed by the addition of SYBR Green I in the micro-tubes. Conventional PCR, Real-time PCR, Nested PCR In this study, conventional PCR, Nested PCR and Real-time PCR were examine on the serial dilution of cloning plasmid that Contains 18s, ITS1, 5.8s and ITS2 region of standards L. infantum, major and tropica strains. Fig. 5 demonstrates the copy number detection threshold for each strains. Conversional PCR detected 4Ã—105, 4Ã—108, and 4Ã—108 of Lishmania DNA for L.infantum, L.major and L.tropica, respectively. Nested PCR detected 4Ã—105, 4Ã—107, and 4Ã—105 of Lishmania DNA for L.infantum, L.major and L.tropica, respectively Real-time PCR detected 400 copies of all Lishmania strains DNA (Fig.5). Fig5: the copy number detection limit of three molecular method for each strains. Real Time PCR was The most sensitive method for detection leishmania strains.

Conclusion: The results showed that Real-time PCR is more sensitive than Nested PCR to detect Leishmania infantum. The LAMP is similar to Real-time PCR for detection of Leishmaniasis and it is more sensitive than other molecular methods. The LAMP assay is a rapid, accurate, and easy method that can be used for detection of leishmania parasites in human and dog samples.

Keywords: Leishmania, molecular detection, Loop mediated isothermal amplification

PECULIARITIES OF SOME ESSENTIAL OIL PLANTS AND DEVELOPMENT OF THEIR GROWTH BIOTECHNOLOGY IN NEWEST WATER STREAM HYDROPONIC CONDITIONS (Research Paper)

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Introduction: Soilless culture of plants, as a new sphere of biological industry, modern biotechnological method of obtaining raw material, enables optimal conditions for plant growth and development, and through headed conditions to obtain more effective, high quality, ecologically clean raw material. In the institute of Hydroponics Problems, NAS RA has been developed and patented a new, modern system: â€œwater-stream hydroponicsâ€ with its varieties (cylindrical, gully, continuous, perennial planting), which is 5-6 times cheaper than classical hydroponics. The bases of water stream hydroponics are the periodical and irretrievable push /in the form of a jet/ of the nutrient solution directly to the root-bearing stratum of the plant, which is automatically regulated from the viewpoint of time and quantity. The research objective is the study of properties of valuable, pharmacologically endowed, essential oil plants (Mentha piperita L., Ocimum basilicum L.) as well as the development of the soilless production biotechnology with enhancing of their effectiveness and secondary metabolites in the newest water-stream hydroponics system. Comparisons were made with classical hydroponics and soil culture.

Methods: In conditions of water-stream hydroponics the plants have been set in cylindrical, gully, continuous systems and in semi-productive beds of hydroponics experimental station with 8 plant/m2 surface. Volcanic red

slag filler with 3-15 mm diameter particles was used in all hydroponics systems. The plants were nourished with G.S. Davtyanâ€™s nutrient solution with 0.5-0.75 N concentration during all vegetation period. In water-stream hydroponics the nutrient solution was pushed irretrievably (6-20 times, with 10-15 second duration) in the form of jet to the root-bearing stratum of the plant during the day. One-time given solution is 20-50 ml depending on weather conditions. In classical hydroponics the plants nutrition was 1-3 times, in soil culture once 3-4 days where the all agricultural rules were kept.

Results: Peppermint and sweet basil, dry, raw material, obtained by using different hydroponic methods, exceeded soil culture 1.4-3.3 times. Essential oil biosynthesis acceleration in both crops was observed in August in case of plant rapid growth. In cylindrical and classical hydroponics, the output of a peppermint essential oil (1.4-2.5 times) was observed due to high yield of plants. In the raw material of sweet basil, increase of essential oil output (1.3-3.0 times) was favorable in cylindrical hydroponics. Almost a similar pattern was observed in case of extracts, flavonoids and tannins.

Conclusion: Essential oil in plants organs is subjected to quantitative and qualitative changes during the vegetation. With high content of menthol (71-73%) from the common elements of essential oil were distinguished in the peppermint grown in cylindrical hydroponics, classical hydroponics and soil culture. In cylindrical hydroponics, which provided maximum essential oil output, menthol maximum content was observed at the end of vegetation, in September (71%) and the lowest content (40%) in August. High content of estragole (30%) in essential oil of sweet basil was also observed in conditions of cylindrical hydroponics in July and August, and linalool high content in August (41%).

Keywords: water-stream hydroponics, Đµssential oil, menthol, productivity, biotech

Polymeric Nanoparticles in Gene Therapy (Review)

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Introduction: With the development of genomic technologies, the prospect for gene therapy has progressed rapidly. The major challenge of gene delivery is to improve the transfection efficiencies of the nonviral carriers. Among various nonviral gene vectors, nanoparticles (NPs) offer an ideal platform for the incorporation of all the desirable characteristics into a single gene delivery system. The field of polymeric nanoparticles is quickly expanding and playing a pivotal role in a wide spectrum of areas ranging from electronics, photonics, conducting materials, and sensors to medicine, pollution control, and environmental technology. Among the applications of polymers in medicine, gene therapy has emerged as one of the most advanced, with the capability to tackle disorders from the modern era. However, there are several barriers associated with the delivery of genes in the living system that need to be mitigated by polymer engineering. For the past few decades, there has been a considerable research interest in the area of drug delivery using particulate delivery systems as carriers for small and large molecules. Particulate systems like nanoparticles have been used as a physical approach to alter and improve the pharmacokinetic and pharmacodynamic properties of various types of drug molecules. They have been used in vivo to protect the drug entity in the systemic circulation, restrict access of the drug to the chosen sites and to deliver the drug at a controlled and sustained rate to the site of action.Various polymers in nanoparticle formulations have been used for pharmaceutical research and gene therapy to increase therapeutic benefits while increasing side effects.

Methods: By reviewing the latest scientific articles, the PubMed site and scientific books have been collected.

Results: Alkylcyanoacrylates can be polymerized in acidified aqueous media by a process of anionic polymerization. The small particles produced tend to be monodisperse and have sizes in the range of 20 to 3000 nm depending upon the polymerization conditions and the presence of additives in the form of surfactants and other stabilizers. The

polyalkylcyanoacrylate nanoparticles so produced have been studied in recent years as a possible means of targeting drugs to specific sites in the body, with particular emphasis in cancer chemotherapy. The small colloidal carriers are biodegradable and drug substances can be incorporated normally by a process of surface adsorption. The review by Davis and others considers the formulation of nanoparticles, the important physicochemical variables such as pH, monomer concentration, added stabilizers, ionic strengths, etc., as well as the characteristics of the particle so created in terms of surface charge, particle size, and molecular weight. Monodisperse particles in the range of 20 to 3000 nm can be obtained.

Conclusion: In addition, by the use of stabilizers such as dextran and its derivatives, which can be incorporated into the nanoparticle surface by a process of polymer grafting, it is possible to make nanoparticles with interesting surface characteristics and different surface charges (sign). The stability of nanoparticles in vitro and their biodegradation in vivo are examined, and the possible formation of toxic products such as formaldehyde is highlighted.

Keywords: nanoparticles, Gene Therapy, Polymeric Nanoparticles, polyalkylcyanoacrylate ,nanoparticles.

Postbiotics and paraprobiotic; applications in food industry (Review)

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Introduction: In the recent years, consumers interests in healthy products has increased, and the high capacity of probiotics to provide beneficial health effects has led to the growth of scientific and commercial benefits as a health-promoting strategy. But since there were some disadvantages found in probiotics, new terms have taken the floor. Paraprobiotics are killed and inactivated forms of probiotics and postbiotics are soluble factors (products or metabolic by-products) secreted by living bacteria (probiotics) or released after bacterial lysis , such as enzymes, peptides, teichoic acids, peptidoglycan-derived muropeptides, polysaccharides, cell surface proteins, and organic acids came to work which have the ability to produce things like bacteriocin and enzymes.

Methods: The term postbiotics can be regarded as an umbrella term for all synonyms and related terms of these microbial fermentation components. Therefore, postbiotics can include many different constituents including metabolites, short-chain fatty acids (SCFAs), microbial cell fractions, functional proteins, extracellular polysaccharides (EPS), cell lysates and pili-type structures.

Results: They also have anti-inflammatory, antimicrobial, immune-modulating and anti-malignant properties. Blood pressure control, obesity control, pathogen cell control and antioxidant properties are some of the effects of postbiotics on body. These postbiotics have drawn attention because of their clear chemical structure, safety dose parameters, long shelf life, lower pathogenic risk, ease of purification and storage in the industry. These biotics are easily absorbed, metabolized and excreted by various host organs and tissues and they are easily absorbed, metabolized and excreted by various host organs and tissues.

Conclusion: These properties show that postbiotics can help improve the hosts health by ameliorating particular physiological functions even if the mechanism hasnâ€™t been clearly determined. The lastest useful programs related to postbiotics have been worked on in order to study safety goals of food. The programs are to keeping, packing of food and

control of the biofilm. During industrial development actions, most of the factors related to food components such as PH, the density of protein, fat and carbohydrates, water activity actions, the presence of natural antibiotics and also processing and storing conditions can influence the probiotic cells losing their power. By this reason, postbiotics are safer and more resistant than probiotics.

Keywords: postbiotics, paraprobiotics, probiotic, immune system, food industry

Preparation and characterization of nanoparticles containing farnesol and evaluation of their in vitro anti-cancer effects in colorectal cancer (Research Paper)

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Introduction: The progression of colon cancer is mainly characterized by a rapid increase in tumor mass and volume (in solid tumors), an invasive increase, and an overall decrease in patient survival. In cancer, autophagy plays a dual role in preventing tumor growth by inhibiting the accumulation of damaged proteins and, on the other hand, promotes tumor growth by helping its cells survive. In tumor therapy, apoptosis tolerance is an important mechanism of tumor resistance to treatment. Autophagy can prevent drug-induced apoptosis and tumor resistance. However, autophagic cell death may also be a form of death for apoptotic tolerant tumor cells. Farnesol is an isoprenoid alcohol obtained from various plants such as citronella,cyclamen, roses, and musk. Its anti-neoplastic effects in various types of human cancers, such as breast cancer, lung cancer, prostate cancer, pancreatic cancer and multiple myeloma, have been investigated by inhibiting cell proliferation in vitro and suppressing tumor growth in vivo. On the other hand, niosomes, which are one of the new drug delivery systems, have received a lot of attention today due to their better penetration and controlled release in position, biodegradable, and biocompatibility with the body. There is currently no effective treatment for tumors among the conventional therapies used because most conventional therapies kill cancer cells but also damage healthy tissue. This

study aimed to evaluate the effect of farnesol-bearing nanoniosome in the treatment of colon cancer.

Methods: Niosome nanoparticles containing farnesol were prepared using a thin-layer hydration method containing a mixture of Span60, and cholesterol in different molar ratios. All formulations were identified in terms of size, entrapment efficiency, release specifications. Sampling was performed for soluble farnesol and niosome containing farnesol for up to 72 hours during specified times (1, 2, 4, 8, 24, 48, and 72). The effect of farnesol-containing nanocarriers on the HT29 cell line of colon cancer was investigated by MTT assay and cell cycle by flow cytometry. The effect of drug containing nanocarriers on the expression of LC3 and ATG genes involved in autophagy was also investigated by Real-Time PCR

Results: According to the morphology of nanoparticles with a SEM microscope, the particles have a uniform spherical structure and suitable size. The optimal sample with a lipid to drug ratio of 30 and a surfactant to cholesterol ratio of 2 was selected under 7 min sonication time. The drug retention efficiency in the sample optimized by the box-Behnken method is 94.57 Â± 1.24. The average size of nanoparticles without Farnesol is 209 nm with a dispersion index of 0.7, which increases to 233 nm when the drug is introduced into the nanoparticle. In the first 6 hours, approximately 85% of soluble farnesol is released and after 48 hours, the release reaches 100%. While the release of the Farnesol-bearing Niosome is a two-step process, the first step is the rapid phase, with 50% of the drug released in the first 24 hours, but after 72 hours the drug release reaches almost 60%. Farnesol-containing nanoniosomes significantly (PvalueË,0.001) reduced the cytotoxicity of the compound and showed higher efficacy than the free drug. The results of this study showed that niosomal nanocarriers containing farnesol had a lethal effect on cancer cells in 72 hours at all concentrations. Flowcytometric studies of Annexin V-PI showed that cell death, early apoptosis of HT29 cells treated with IC50 nanoparticles containing farnesol increased by about 12% after 48 hours compared to the control group. The results of cell cycle analysis showed that about 24% of the cells were treated in the sub G1 stage as a result of treatment with biological nanoparticles. The increase in cell accumulation in the sub G1 stage compared to the control group was statistically significant (PvalueË,0.001). On the other hand, a significant decrease was seen in the cell population located in the G2 stage compared to the control group. In

the expression of genes involved in autophagy (LC3, ATG) increase in expression was seen compared to the control group (PvalueË,0.001).

Conclusion: According to the results of this study, Niosome containing farnesol with desirable characteristics induced apoptosis; Autophagy in cancer cells and increase the lethal effect on cancer cells. As a conclusion, it can be a good candidate for the treatment of colon cancer.

Keywords: Farnesol ,colorectal cancer, Autophagy

Production and characterization of recombinant human leukemia inhibitory factor and evaluation of anti-fertility effects of rabbit anti-rhLIF in Balb/c mice (Research Paper)

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Introduction: Human leukemia inhibitory factor (hLIF) is a cytokine of interleukin-6 family. This study aimed to evaluate the recombinant production rate of active hLIF by different vector-host systems under various conditions. Moreover, a rabbit polyclonal antibody (pAb) against recombinant hLIF (rhLIF) was produced and its anti-fertility effects were explored in Balb/c mice.

Methods: Four different constructs including pET22b/hLIF, pET28b/hLIF, pET32b/hLIF and pColdI/hLIF were designed and transformed into BL21-(DE3), Rosetta-(DE3), Origami-(DE3) and Shuffle T7-(DE3) host cells. The expression level and proliferative effect of rhLIF were measured by SDS-PAGE and MTT assays, respectively. Rabbit pAb to rhLIF was produced and characterized using enzyme-linked immunosorbent assay and western blot techniques. The Balb/c mice were divided into two intervention and control groups. Then, they were intraperitoneally injected by purified rabbit anti-rhLIF and non-immunized rabbit pAb, respectively. After sacrifice on day 7, the number of implantation sites was counted.

Results: The rhLIF was successfully expressed by pET32b/hLIF and pColdI/hLIF vectors in all hosts with no significant difference in the rate of

their expression. The rhLIF was purified and checked for activity. The results showed that it is functionally active and the produced anti-rhLIF pAb could specifically bind to commercial rhLIF. Passive immunization results showed that anti-rhLIF antibody completely inhibited fertility in all injected Balb/c mice compared to controls

Conclusion: Although previous studies showed expression of rhLIF using various methods, using different vector-host systems ensures us of successful biological active expression of it. The pAb against rhLIF could be a powerful tool for inducing in vivo infertility.

Keywords: Leukemia inhibitory factor, Anti-ferti, Recombinant protein, pET32b/hLIF vector, pColdI/hLIF vector

Production of hydrocolloid-based moisturizing cream in Nostoc cyanobacteria (Research Paper)

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Introduction: Hydra-Soothing fluid, a non-greasy moisturizing milk, repairs and nourishes skin with shea butter and apricot kernel oil. It contains a wide range of chemical compounds such as emollients, occlusives and humectants to absorb, retain and increase efficiency to prevent water evaporation or transepidermal (TEWL). However, as a result of the use of chemicals in the composition of these hydrating products, various allergic reactions may occur on the surface of the skin. On the other hand, the accumulation of these substances on the surface of the skin pores can sometimes block the skin pores and cause various complications that eventually cause a hydrophobic barrier on the skin. The potential use of cyanobacteria as hydrating agents in cosmetics stems from the fact that these organisms have protective mechanisms, including the production of exopolysaccharides (EPS), which enable them to withstand deficiencies or Resist water loss. Cyanobacterial exopolysaccharides are formed by various sugars and uric acids, of which more than 60% may be dry weight. In cells, EPS can be covalently attached to the cell surface to form sheaths, capsules, and mucosa. Tolerance of cyanobacteria to salinity in highly saline environments appears to be due to the presence of a thick EPS layer around the cells. Also, in some studies, it was found that the group of Nostoc cyanobacteria, which contain small amounts of EPS, have a high tolerance against drought and water shortage, so that this feature of drought tolerance and water retention in the preparation of health and moisturizing creams Therefore, the objectives of this study are to produce a hydrating cream based on natural ingredients and bioactive compounds (active ingredient or hydrocolloid) in Cyanobacterium nostoc and to evaluate the antibacterial properties against Pseudomonas aeruginosa.

Methods: Nostoc cyanobacteria were collected from the coastal and southern areas of the North Sea of Iran. Extraction was performed by three methods: methanolic, hexane and aqueous. Pseudomonas aeruginosa ATTC1430 was cultured on nutrient agar medium and MÃ¼ller-Hinton agar medium half McFarland standard containing 1.5Ã— CFU / ml was prepared. Also, the antibacterial effects of Nostoc extract were investigated using disk diffusion and welling methods. Then the extraction of the active ingredient Hydrocolloidia as well as the formulation of the hygienic cream and the amount of hydration were performed using different concentrations and then the results were read by the Dinolait digital hand microscope model AM211. The data analysis method was used to evaluate the properties and characteristics of the creams produced in such a way that the values obtained from measuring viscosity and pH were statistically analyzed using SPSS 14.00 computer software in Windows 2016 environment

Results: The results of the present study showed that the effect of Nostoc cyanobacterial extracts on Pseudomonas aeruginosa was such that the diameter of the growth inhibition zone was 20 mm in aqueous extract, 30 mm in methanolic extract and 25 mm in hexane extract, as methanolic extract was the most abundant. It has an inhibitory effect on bacterial growth and has caused the death of Pseudomonas aeruginosa. The lowest concentration as the minimum concentration of bacterial growth inhibitor was 0.6 mg / ml and the same concentration was obtained in the study of the minimum lethal concentration.

Conclusion: It should be noted that the lowest growth inhibitory concentration was observed in hexane extract 0.59 and in aqueous extract 0.55 mg / ml. In one gram of cream, the skin has the highest amount of hydration, and the properties and characteristics of creams produced by creams such as viscosity and pH increased with increasing duration of use. Also, the largest size of the growth inhibition halo is related to the combined sample of the produced cream and the hydrocolloid of Cyanobacter Nostoc. The size of the non-growth halo diameter of the composite sample in the disk diffusion method is 25 mm larger than the diameter of the halo created in the well drilling method is 23 mm. 0.49 mg / ml and the composition of the cream produced and the hydrocolloid Cyanobacterium nostoc is equal to 0.38 mg / ml. Therefore, it can be acknowledged that Cyanobacterium nostoc has a good antibacterial effect against Pseudomonas aeruginosa.

Keywords: Antibacterial, Cyanobacterium nostoc, Exopolysacharids ,Pseudomonas aeruginosa and Moisturizing Cre

Production of moisturizing cream using Nostoc cyanobacteria and its antibacterial effects (Research Paper)

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Introduction: Following the increasing bacterial resistance to common commercial antibiotics, the trend The use of natural compounds with antibacterial and antimicrobial properties has increased and cyanobacteria are a good source of sunscreens and moisturizers. Currently, the global production of microalgae and cyanobacteria is mainly aimed at high value-added applications as algal biomass contains pigments, proteins, fatty acids, polysaccharides, vitamins and minerals, all of which are of interest. They have a lot to do with natural products, both in food and in cosmetics. Therefore, in this study, the possibility of producing moisturizing cream by Nostoc cyanobacteria and studying its antibacterial effects on Pseudomonas aeruginosa has been investigated.

Methods: Nostoc cyanobacteria were collected from the coastal and southern parts of the Caspian Sea in the direction of water flow. And growth of Nostoc cyanobacterial strain of Zindro liquid extraction medium was prepared by aqueous, methanolic and hexane methods. Bacterial culture was performed in nutrient agar medium and MÃ¼ller Hinton agar medium and half McFarland tube was used to standardize the microbial suspension protection. Took. Then, the extraction of hydrocolloids and the intention of the hygienic cream formulation and the amount of hydration were performed using different concentrations, and then the results were read by the Detolite digital hand microscope, model AM211.

Results: The results of the present study showed that the effect of Nostoc cyanobacterial extracts on Pseudomonas aeruginosa was such that the diameter of the growth inhibition zone was 20 mm in aqueous extract, 30 mm in methanolic extract and 25 mm in hexane extract, as methanolic extract was the most abundant. It has an inhibitory effect on bacterial

growth and has caused the death of Pseudomonas aeruginosa. The lowest concentration as the minimum concentration of bacterial growth inhibitor was 0.6 mg / ml and the same concentration was obtained in the study of the minimum lethal concentration.

Conclusion: It should be noted that the lowest growth inhibitory concentration was observed in hexane extract 0.59 and in aqueous extract 0.55 mg / ml. In one gram of cream, the skin has the highest amount of hydration, and the properties and characteristics of creams produced by creams such as viscosity and pH increased with increasing duration of use. Also, the largest size of the growth inhibition halo is related to the combined sample of the produced cream and the hydrocolloid of Cyanobacter Nostoc. The size of the non-growth halo diameter of the composite sample in the disk diffusion method is 25 mm larger than the diameter of the halo created in the well drilling method is 23 mm. 0.49 mg / ml and the composition of the cream produced and the hydrocolloid Cyanobacterium nostoc is equal to 0.38 mg / ml. Therefore, it can be acknowledged that Cyanobacterium nostok has a good antibacterial effect against Pseudomonas aeruginosa.

Keywords: Antibacterial, Cyanobacterium nostoc, Pseudomonas aeruginosa and Moisturizing Cream.

Recombinant expression of bovine enteropeptidase light chain in SHuffleÂ® T7 Express as a new host and optimization of induction parameters (Research Paper)

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Introduction: Enteropeptidase is an enzyme consists of two subunits including heavy chain and light chain. The light chain of enteropeptidase (EPL) is the proteolytic subunit that specifically recognizes (Asp)4-Lys amino acid sequence and cuts after lysine amino acid. Due to the importance of this enzyme in laboratory and industry for purification of expressed protein in fusion with a fusion tag, a lot of study has performed on the EPL expression using different prokaryotic and eukaryotic expression hosts including yeasts and Escherichia coli. SHuffleÂ® T7 Express is an engineered strain of E. coli that is valuable for the expression of proteins that contain disulfide bonds to form the protein correctly. It is also capable of refolding mis-oxidized bonds to form in a correct way. Enteropeptidase light chain contains multiple disulfide bonds in its structure and it is indicated that it is a hard to express protein. In this research, we applied the SHuffleÂ® T7 strain and we evaluated the potential of this strain as a new host to express and correct folding of EPL. We subcloned the DNA encoding EPL into pET-32b plasmid in frame with thioredoxin tag that is a solubilization enhancing factor. Then, we evaluated the proteolytic activity of purified EPL and expression condition optimized using response surface methodology (RSM).

Methods: Vector and bacterial culture media: Subcloning was performed by restriction cloning. Amplifying the EPL DNA sequence was done by PCR using pET-28a plasmid containing the DNA sequence of EPL as template. The amplified sequence was then inserted into pET-32b. Chemical transformation and expression: Standard protocol of Chemical method was applied to prepare competent cells. After overnight cultivation of a transformed colony, one ml of the cultivation was added to fresh medium

in a volume of 100 mL containing 100 Âµg mL-1 ampicillin and incubated at 37 Â°C in a shaker incubate with the speed of 160 rpm to reach the OD600 of 0.8. Then, 1 mM IPTG was inoculated to induce protein expression and incubation was continued for four h. Extraction of expressed protein and purification: After extraction by lysis buffer containing 1 mgr/ml lysozeme, Urea gradient was exerted to solubilize and recovery of protein structure from inclusion bodies. Then, Ni-NTA purification system was used to purify the protein. Biological assay: Using different value and ratio of the EPL to its substrate (Thioredoxin/hGH fusion protein), the activity of EPL was assayed and incubation of reaction tubes was done at 37 Â°C for 12 h. Parameters optimization using RSM optimization approach: Central composite design (CCD) was used to optimize the significant factors for protein expression including temperature, the concentration of inducer, incubation time and OD of induction.

Results: Cloning of EPL DNA in pET-32b: EPL DNA was amplified from pET-28a by PCR and cloned correctly into pET-32b by restriction cloning. Expression and purification: Primary analyze was indicated that inclusion bodies were formed. Solubilization of inclusion bodies was performed by urea gradient method. The concentration of purified protein was 200 microgram/ml. Biological assay: The results indicated that the substrate was digested by proteolytic activity of EPL into two protein fragments thioredoxin and hGH. Optimization of enteropeptidase production: Optimized parameters were 1.05 mM inducer, OD of induction 0.6, seven hour incubation after induction, and 26.5 Â°C for temperature. The yield of expression in this condition was 1780.85 Âµg mL-1 that is a high level of expression.

Conclusion: In this research, expression and RSM optimization of EPL was conducted and the active enzyme was achieved. Before optimization, a comparable expression value with previous researches was achieved. Optimization resulted in the high level of protein expression (1780.85 Âµg mL-1) in the condition of 1.05 mM inducer (IPTG) at OD: 0.6 and seven h incubation at 26.5 Â°C for EPL. However, using SHuffleÂ® T7 Express as a capable strain in correct folding of protein was not effective on the cytoplasmic expression in soluble form.

Keywords: Enteropeptidase light chain, SHuffle T7 Express, parameter optimization.

Sensitizer drugs, intelligent response of medical biotechnology to diseases: focus on Levosimendan (Research Paper)

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Introduction: Drugs such as Nitroglycerin were once among the most widely used drugs in humans, although they are still widely used in parts of the world, but the spread of biotechnology has moved them from home drawers to hospital emergency shelves. Human beings have learned from biotechnology that should use non-invasive methods for their treatment, sensitizing drugs are one of the newest non-invasive drugs and alternatives to today's common drugs for the treatment of diseases such as hypertension, heart disease and diabetes. in this essay we examine the Levosimendan performance.

Methods: Our method in this research has been to use articles published in scientific research journals, dissertations, reference books in the field of medical sciences as well as approved case reports.

Results: Levosimendan is used in patients with acute heart failure (AHF). In these patients there is congestive heart failure, as a result of which cardiac output is significantly reduced. Decreased cardiac output in these patients causes shortness of breath and pain when breathing. Levosimendan, with its combined effects, rapidly reduces pulmonary stenosis and improves blood flow to various parts of the body, including the kidneys. It also increases Glomerular filtration rate (GFR) by improving blood flow to the kidneys. Levosimendan increases the sensitivity of the heart to potassium ions. It is necessary to monitor the amount of potassium in the patient's body before injecting Levosimendan to prevent the possible effects of cardiac arrhythmias.

Conclusion: This drug can be an effective and efficient alternative to beta-blockers. Levosimendan promote heart to Natural work and absorb more calcium as a result have a better output without multi organ Complications and block receptors.

Keywords: Levosimendan, Heart, cardiac output, Beta-Blocker

Stem cell transplantation: a clear horizon for therapy of Multiple Sclerosis (Review)

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Introduction: Multiple sclerosis (MS) is an autoimmune-based demyelinating disorder of the brain and spinal cord, which finally made an axonal loss and eternal neurological disability. Epidemiologically, MS is the most common demyelinating disease, with a prevalence that varies extremely, from a high rate of prevalence in North America and Europe (>100/100,000 inhabitants) to a low level in Eastern Asia and south of the Sahara in Africa (2/100,000 population). Although recent proof suggests that MS relapses are created by environmental and exogenous triggers like the infectious agent and genetic background, its very complex pathogenesis is not completely understood. Therefore, the utility of current immunosuppression-based therapies of MS is too low. Cell-based therapies have provided a new chance for the prevention and treatment of different neurodegenerative diseases like MS. In this review, we discuss the current datum, methods, and limitations of stem cell-based therapies for the treatment of patients with MS.

Methods: A comprehensive search was performed in electronic databases PubMed, Scopus, Science Direct, UpToDate, and Web of science with the keywords â€œStem Cellâ€ and â€œMultiple Sclerosisâ€ from 2012 to 2020. Original articles that mentioned the therapeutic effects of stem cells on MS were included in the study.

Results: Currently, existing treatments for MS help ameliorate the patientâ€™s overall quality of life and reduce long-term disability by preventing the recurrence and severity of MS attacks, however, so far there is no cure for this disease. In recent years, stem cells derived from a variety of sources have been used in clinical trials as transplant agents to break down and alter the faulty chemical process or damaged tissue. The foremost common kind of stem cells used in the treatment of MS is

mesenchymal stem cells (MSCs) found within the bone marrow because of their harmlessness and straightforward extraction ways. In addition to mesenchymal cells, there are other types of stem cells that can be used for the treatment of MS. Autologous hematopoietic stem cell transplantation (HSCT) is another method that can be considered as a therapeutic option. The goal of HSCT is to remove stem cells and modulating the patientâ€™s immune system to attain long-run remission of MS. Umbilical cord (UC) stem cells are also an effective treatment for MS due to their high ability to differentiate into diverse tissue. However, a cell bank is required to reserve and sustain these cells. Adipose tissue stem cells (ASCs) are one of the best types of stem cells that can be used in the treatment of MS. Firstly, the sequestering of the fat tissue is straightforward and might be provided from various organs of the body. Secondly, the density of stem cells per unit of area in fat tissues is high and during sampling, a large number of stem cells can be obtained. Thirdly, the cost of stem cell transplantation from fat tissue is negligible. Meantime, adipose MSCs, like the adult stem cell group, are looks safe to use. These benefits make the ASCs an acceptable candidate for the treatment of MS. Neuronal stem cells can also be a source of well-differentiated cells that can be quickly altered by damaged neuronal cells. However, this methodology requires a high number of aborted fetuses that create it terribly arduous for preparing needed cell stem cells.

Conclusion: Studies have shown that cell therapy significantly improves the quality of life, neurological disability, and functional scores. In general, HSCT and MSC transplantation in MS patients have been well-tolerated, but several potential acute and chronic adverse effects should be considered. Infusion-related toxicity and infection are serious risks of stem cell therapy, and additive immunosuppressive treatment increases the risk of infection after transplantation. Ectopic tissue formation and malignant transformation of stem cells are theoretical concerns, although it has not been reported in MSC therapy studies, yet. Well-designed randomized controlled studies that systematically evaluate the efficacies and safety of cell replacement therapy compared to other relevant treatments are needed to clarify treatment benefits.

Keywords: Stem cell, Multiple Sclerosis, Stem cell therapy

Structural analysis and engineering of industrial alpha-amylases (Review)

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Introduction: Enzymes are a suitable alternative to catalysts in various industries due to their specificity, performance under milder conditions, and reduced production of by-products as a result of the reaction. The carbohydrases, as enzymes that catalyze the conversion of carbohydrates into simple sugars, are a pioneer in the global industrial market. The alpha-amylase enzyme is the most widely used carbohydrate in various industries such as detergent, food, poultry feed, textile, paper, and fuel production. Bacterial- and the fungal-derived Alpha-amylases are widely used in industry due to their high efficiency, and pH, and thermal stability. four important characteristics of alpha-amylases in the industry are calcium dependency, thermostability, pH profile, and oxidative resistance of enzyme. Extensive efforts have been made to optimize the activity of the enzyme in industrial conditions. But, none of the known wild-type alpha-amylase has been in the optimal state for all the mentioned above features together so far. Therefore, in recent years, many attempts have been made to produce the ideal alpha-amylase through protein engineering methods. Optimization of enzyme activity conditions and also enzyme engineering often requires accurate knowledge of the structural origin of the desired properties. Therefore, In the present study, the sequence alignment between 6 industrially important alpha-amylases was performed. Sequence alignment results were used for molecular analysis and investigation of the structural origin of their industrially important features.

Methods: In this review, we summarize the findings from various studies related to structure, enzyme engineering, and industrial application of alpha-amylase through a comprehensive PubMed, Science Direct, and Google Scholar search. The keywords "industrial enzyme"," microbial enzyme", "alpha-amylase", "enzyme crystallography", "calcium

dependency", "thermostability", "pH profile" and "oxidative resistance", "enzyme engineering "were entered into the search field and 50 articles were investigated between the years 1990-2021. Also, in another part of this study, we explored the relation of sequences and structure with four important features of alpha-amylase via bioinformatics approaches. The amino acid sequences of six-industrially important alpha-amylase were obtained from NCBI and UniProt database. The sequence alignment was performed by ClustalÏ‰ software. Then, the ESPript3.0 program was used to visualize the alignment for the publication purpose. Sequence alignment was analyzed by Jalview software. The 3D structures of the enzymes were obtained from the PDB database and visualized by PyMol and Chimera software. the atomic distances were measured using Chimera software.

Results: The overall structure of alpha-amylases consists of three domains A, B, and C. Domain A is the most conserved domain among all alpha-amylases, consisting of three catalytic residues and a fully conserved calcium-binding site which is essential for maintaining the function and stability of the enzyme structure. Domain B is the least conserved domain and this variation is one of the factors that develop unique properties in thermostable alpha-amylase. The second calcium ion together with the other calcium and a sodium ion forms a metal-triad that plays an important role in the thermostability of the alpha alpha-amylase of B.licheniformis, B.stearothermophilus, and B.amyloliquefacions. However, the binding site of the second calcium ion in A. niger and A. oryzae alpha-amylases is catalytic residues, and the presence of excess amounts of this ion will lead to a significant decrease or loss of enzyme activity. The binding site of the third calcium ion with the least conservation plays a mainly structural role. In the thermostable alpha-amylases a loop containing 21 residues, is one of the main factors besides metal-triad in developing thermal stability. Factors determining the pH profile of alpha-amylase mainly affect the pKa of catalytic residues by changing the electrostatic field. However, the dynamics of catalytic residues also play a role in determining their pH profile, which is more complicated. Under oxidative conditions, the oxidation of the amino acids methionine and cysteine present at the surface of the enzyme structure, especially near or inside the active site cleft, increases the volume of these residues, resulting in a dramatic decrease in enzyme activity.

Conclusion: Understanding these structural factors leads to the optimal use and engineering of alpha-amylase for industrial application. This

knowledge will help researchers with efficient enzyme engineering and developing optimized industrial alpha-amylases and thus enhancement of efficiency which leads to the reduction of additional costs in the industry.

Keywords: alpha-amylase, industrial enzyme, microbial enzyme, enzyme engineering

Structural Analysis of the Globins Binding Sites (Research Paper)

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Introduction: Globins are a superfamily of proteins that bind to an organic molecule heme. These proteins are present during evolution from prokaryotes to eukaryotes and have important biological functions such as Oxygen transfer and storage, nitric oxide (NO) metabolism, detoxification of reactive oxygen species (ROS), protection against apoptosis, signal transduction, etc. (Keppner et al., 2020; Buemester and Hankeln , 2014). Globins are structurally in the form of a 3-on-3 Hb fold, also known as myoglobin-fold, and 2-on-2 Hb fold, which belong to the family of Truncated hemoglobins (TrHb). Each of these folds is known to provide different binding affinities to the globins target molecules. As a result, structural studies of the globins binding sites can help us to study their interactions with Oxygen in different organisms. We can also suggest strategies for optimal use of these proteins in genetic engineering and life sciences. Thus, we examined the structure of binding sites in the main 6 groups of globins that were selected from different families to find the best energetically favourable interactions between globin and heme.

Methods: We used PDB to select the three-dimensional (3D) structures of the globins (http://www.rcsb.org/). To select the structures, we considered the best resolution heme-bound structures with the least number of missed amino acids to examine the interactions more accurately and completely. In the next step, we examined all the atomic interactions within 5 Çº of the heme-binding site using PYMOL biomolecular visualizer (WL, 2002).

Results: While examining the interactions in all of the 6 selected groups of globins, we divided them into 4 categories: 1- Histidines that are known to

play an essential role in heme binding 2- Charged amino acids 3- Polar amino acids 4- non-polar amino acids. The results of comparing these structures showed us that myoglobin and leghemoglobin have the best binding energy with heme molecule among all the six studied groups. The difference in the biding site is mainly driven by the number of Histidines and other charged amino acids. Both myoglobin and leghemoglobin have three Histidines which is the highest number and the highest number of charged amino acids which is two in their binding site. These are His64, His93, His97, Lys42, Lys45 For myoglobin and His63, His97, His106, Lys66, Lys100 for leghemoglobin binding sites. Based on our observations, myoglobin and leghemoglobin will have stronger interactions with heme. And these results are consistent with previous studies on globins.

Conclusion: By studying the structural binding sites of the most important groups of globins we showed that leghemoglobin can have a stable interaction with heme molecules such as myoglobin. Thus, leghemoglobin is a potential target for myoglobin replacement in the use of industrial-scale recombinant protein production processes to improve respiratory efficiency, genetic engineering approaches involved in oxygen supply in culture medium and agriculture.

Keywords: Globins, Heme, Binding Site

Study the effect of RG108 small molecule on neural differentiation of adipose tissue-derived stem cells (Research Paper)

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Introduction: Recent findings suggest the possibility of using epigenetic modifiers to reprogram somatic cells and to increase differentiation potential of stem cells. In the present study, small molecule RG108 was used to improve neural differentiation of adipose tissue-derived stem cells (ADSCs).

Methods: Human ADSCs were isolated enzymatically from adipose tissue samples obtained by abdominoplasty and were characterized. The cells were treated with concentrations of 0, 5, 25, and 50 ÂµM RG108 for three days. Then, the effect of different concentrations of RG108 on proliferation rate and cell cycle progression was evaluated by MTT assay and flow cytometry. Also, the expression of OCT4 pluripotency marker was evaluated by flow cytometry. Finally, after 3 days of RG108 treatment, the cells were differentiated for 10 days in a medium consisting of DMEM, 1% FBS, B27, BHA, KCL, forskolin, valproic acid, hydrocortisone, and insulin. Ten days after the initiation of differentiation, the expression of PAX6, NESTIN, NSE, NeuN, NEFL mRNAs and TUJ1, MAP2, TH, proteins was evaluated.

Results: According to flow cytometry results, CD73, CD90, and CD105 markers were expressed in more than 99% of the ADSCs and the cells showed adipogenic and osteogenic differentiation. Treatment with 5 ÂµM

RG108 decreased proliferation rate and frequency of the cells in S phase of cell cycle and upregulated the expression of OCT4 pluripotency gene. Also, treatment with 5 ÂµM RG108 before neural differentiation increased the expression of PAX6, NESTIN, NSE, NeuN, NEFL mRNAs and TUJ1, MAP2 and TH proteins.

Conclusion: The findings of the present study indicated the importance of RG108 small molecule in improvement of neural differentiation of ADSCs which may be beneficial for application of these cells in cell therapy of neurodegenerative diseases.

Keywords: Adipose tissue stem cells, reprogramming, RG108 small molecule, neural differentiation

Survey on Efficiency of inoculation methods of Pseudomonas fluorescens on growth and yield of Thymus kotschyanus (Research Paper)

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Introduction: The use of microorganisms as biofertilizers for improve crops and production has been used and being common practice in the last years. Plant growth-promoting rhizobacteria (PGPR) (Kloepper, 1993) has known as biofertilizer because these microorganisms adapt and grow rapidly around plant rizosphers (Ahirwar et al., 2015; Ul Hassan and Bano, 2015). However, some reports indicate that rhizobacteria inhibit the maximum growth of some plants by producing hydrogen cyanide. Research has shown that growth-promoting soil bacteria can increase plant growth and mineral uptake. Facilitate even in stressful situations [6]. Pseudomonas fluorescens can cause of increase the plant's access to absorbable iron in the rhizosphere and subsequently play an important role in improving plant growth in terms of quantity and quality. they are famous biofertilizers and also through various mechanisms such as stimulating the production of plant hormones such as auxin, cytokine and gibberellin and also inhibiting the production of ethylene, increasing the solubility of inorganic and organic phosphate, producing microbial siderophores to increase plant access to absorbable iron, nitrogen fixation in symbiotic Or non-symbiotic in stimulating and improving plant growth in terms of quantity and quality

Methods: In this study to investigate Efficiency of various Inoculation Methods of Pseudomonas fluorescens on growth, characteristics and percentage of essential oil of Thymus kotschyanus, an experiment was conducted in Randomized Complete Block Design with four treatments and three replications at Alborz Research Complex, Research Institute of Forests and Rangelands. The standard bacterial strain of Pseudomonas fluorescens (R-169) was obtained from the Soil and Water Research Institute. Method1 :Thymus seeds were placed in a sterile plate. after

determining the germination potential, each seed soaked in 5 ml of bacterial liquid suspension of Pseudomonas fluorescence standard strain (P-169) prepared by the Soil and Water Research Institute with a population of 108cfu / ml was added. For better effectiveness, Arabic gum as a carrier was added for seed adhesive. Before inoculation, Bacterial suspension prepared in 108 cfu / ml at room temperature (25 Â° C) on a shaker at 120 rpm.Then, after 48 hours of incubation, constant turbidity with absorption of 560 nm was read by spectrophotometry. Method2: After rooting the seedlings, 50 ml of the bacterial suspension with 108 cfu / ml by sterile syringe in the zone around the root in contact with rhizosphere of the plants were added. The suspension was prepared and the turbidity was fixed as in the first method. Method 3 Both site inoculation: Bacterial suspension with population of 108 cfu / ml was added by half McFarland method in Erlenmeyer 100 ml with physiological serum in a ratio of 1 to 9 to reach a population of 107 cfu / ml then as in the first method (5 ml per seed) And the second method (50 ml in contact with plant roots) was added. plants harvested after 3 months from transplanting. The oil content was estimated by steam distillation using Clevengerâ€™s apparatus.

Results: In all Inoculation methods, Pseudomonas fluorescence showed, an increase in growth and the amount of essential oil . The effect of inoculation by mixed method (roots and seeds) had a greater effect on morphological traits and growth and percentage of thyme essential oil. The highest amount of root volume with 30 ml compared to the control (15 ml) was significant at the level of 0.5, the highest dry weight of the plant with 24.75 g and the highest number of branches with 25, respectively, compared to the control (20 g and 18 g). Showed no significant difference, and the highest amount of essential oil with 1.74% was obtained in inoculation of Pseudomonas fluorescens in the third method (seeds and roots).

Conclusion: in this study, inoculation of Pseudomonas fluorescence by liquid suspension method with seeds, roots and rhizosphere of the plant had a positive effect on morphological characteristics and percentage of Thymus kotschyanus essential oil, which had a significant effect on some characteristics. The increased fresh and dry weight and root volume of roots in comparison with control was observed. the most effective inoculant method was the both inoculation with seed soaking and roots injection in method 3 in compared to inoculation seperately.

Keywords: Pseudomonas fluorescence, Medicinal Plants, Biofertilizers, Thymus kotschyanus , Bacterial Inoculant

The Advances of Poly-ADP-Ribose Polymerase Inhibitors use in Breast Cancer Targeted Therapy: A comprehensive literature review study (Review)

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Introduction: Today the breast cancer becomes one of the most prevalent cancer all over the world. According to the importance of this cancer, different therapeutic strategies have been developed and developing to find effective therapies for patients suffering from breast malignancies. In this case, targeted therapies have been evaluated as a cost-benefit method in which the specific molecules, receptors, pathways, etc been targeted by the applied agents. Poly (ADP-ribose) polymerases (PARPs) are a group of critical enzymes that involve in the DNA-damage repair. So, it seems that PARPs inhibitors can be effective agents for targeting some specific malignant cell lines. Therefore, in this literature review study, we investigated the last findings and developments about the use of PARPs inhibitors in breast cancer targeted therapy.

Methods: A comprehensive search was conducted in electronic databases Embase, Pubmed, Scopus, and Web of Science, the keywords â€œBreast Cancerâ€, â€œPoly (ADP-ribose) polymerasesâ€ and all MeSH related words since 2010. We included original and review studies for more evaluation in our study. Also, the references of the review studies were checked to reduce the chance of missing any related article.

Results: The investigations determined that PARPs inhibitors are effective agents in targeting triple-negative breast cancer, BRCA 1 associated breast

cancer, and BRCA 2 associated breast cancer. Moreover, this kind of targeted therapy can attack the cancer cells without high levels of cytotoxicity, and also these agents selectively targeting cells with the unstable genome. The last clinical trial studies indicated that several PARPs inhibitor agents are registered; including Olaparib, Talazoparib, Niraparib, Rucaparib, and Veliparib. In detail, Olaparib is determined as an agent for gBRCA1/2+ Advanced solid tumors in all genders. Veliparib is determined as an agent for gBRCA1/2+ and HER 2â€“ basal-like breast cancers but this agent is applicable for more than 19 years old patients. Similar to Olaparib, the Talazoparib is designed for gBRCA1/2+ breast cancers but it can be used in metastatic cancers. Niraparib and Rucaparib commonly targeting gBRCA1/2+ breast malignancies but in some cases, Rucaparib can be effective on HER 2- breast cancers after chemotherapy. It should be noted that the combinations of PARPs inhibitors targeted therapy with other cancer therapies strategies indicated contradictory results that in several combinations high level of cytotoxicity was observed.

Conclusion: Based on our findings, PARPs inhibitor agents can potentially be used in targeting breast cancer cell lines but further clinical trial studies are needed to prove their application in breast cancer patients.

Keywords: PARP, Breast Cancer, Targeted Therapy

The Application of Chimeric Antigen Receptor T-cell Immunotherapy in Breast Cancer Therapeutic Strategies: A literature review study of the current knowledge (Review)

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Introduction: Today Breast cancer has become the most common malignancy among women all over the world. According to the last studies, it was estimated that more than 2.3 million new cases were in 2020. This high prevalence rate of breast cancer made it a highlighted topic in cancer researches. Although different therapeutic methods have been applied against breast cancer up to now, but the Chimeric antigen receptor (CAR) T-cell therapy is novel innovative immunotherapy in which autologous T-cells are genetically modified to express chimeric receptors encoding an antigen-specific single-chain variable fragment and costimulatory molecules. Based on our current developments, CAR T-cell therapy can be used for hematologic malignancies; however, it seems that this effective therapeutic method can potentially be used in solid tumors treatment such as breast cancer. Therefore, in this literature review study, we discussed the last discoveries about CAR T cell therapy in breast cancer treatment.

Methods: A comprehensive search was conducted in electronic databases Embase, Pubmed, Scopus, and web of science with the keywords â€œCAR T-cellâ€, â€œBreast cancerâ€ and all other related MeSH words since 2010. Original and review studies that were discussed about the application of CAR T cell therapy in breast cancer included for further investigations.

Results: According to our comprehensive review of the current knowledge, different studies have been developed for targeting HER2 by CAR T-cells. Also, other targets such as cMET, triple-negative breast cancers, mesothelin, CEA, carbonic anhydrase IX (CAIX), FR-Î±, CD171, GD2, EGFRvIII, fibroblast activation protein (FAP), and vascular endothelial growth factor receptor 2 (VEGF-R2) could be considerable in CAR T-cell therapy. Although CAR T-cell therapy can have incredible therapeutic

effects on malignant cell lines specifically, but some concerns are being existed about its toxicity. In detail, some studies indicated CAR T-cell toxicity as its high expansion in targeted cells. Unfortunately, systemic inflammatory response syndrome or cytokine storm, in which significant release of IFN-Î³, TNF-Î±, IL-2, IL-6, and etc occurs, is the other concern about CAR T-cell therapy. It is notable that some studies indicated that the combination of CAR T-cell therapy with other types of cancer therapies such as target therapy can potentially be more effective and better outcomes can be observed in these cases in comparison with a single therapeutic method.

Conclusion: Despite CAR T-cell is applied for hematologic malignancies treatment, but its potential role in the management and solid cancers therapy is still under study. Further evaluations are needed to investigate the therapeutic or non-therapeutic effects of this type of cancer immunotherapy in solid cancers, especially breast cancer.

Keywords: Immunotherapy, Breast cancer, CAR T-cell

The association between Multiple Sclerosis and Vitamin D status: a review (Review)

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Introduction: Multiple sclerosis (MS) is a complex demyelinating autoimmune disease in which an immune response of the bodyâ€™s immune system is against the central nervous system (CNS). Vitamin D influence on immune cells has been suggested in numerous investigations. Several observational studies have proposed that there is a positive correlation between serum vitamin D deficiency and the development of MS. This study was aimed to review the role of vitamin D in the treatment of MS and with the hypothesis that high levels of vitamin D could be beneficial for MS.

Methods: This review was performed within English articles published at PubMed from 2012 to 2020. The keywords were Multiple Sclerosis, Vitamin D, and clinical trials. By searching this database, 53 articles were found and 36 of them by reading abstract were removed.

Results: Finally 17 articles were included in the study. Many clinical studies and animal models have shown the positive effect of Vitamin D and its metabolites on immune cells that decrease the MS developing by shifting cytokines ratio towards an anti-inflammatory state. Moreover, At least 10 studies have suggested that the cholecalciferol supplements can be used for the treatment of MS, and high vitamin D status reduces the risk of exacerbations and magnetic resonance imaging activity in people with MS, so it makes a significant difference in the patient's quality of life. Although some other studies declare that no strong evidence between positive effects of vitamin D supplements and MS has yet. Also, these studies reported the side effects of high doses of vitamin D supplementation, such as seizures, severe hypercalcemia, kidney failure, gastric symptoms, weakness, and fatigue. Indeed, these side effects develop in patients who intake more than 50,000 IU of cholecalciferol per day over several months.

Conclusion: While observational reports have indicated that vitamin D may reduce inflammation in MS patients, randomized controlled trials have yet to validate this. However, results from clinical trials suggested that vitamin

D doses ranging from 10,000 to 40,000 IU/day appear to be safe as an add-on therapy. The findings highlight the importance of becoming aware of the possible adverse side effects of vitamin D supplementation. Furthermore, no evidence shows vitamin D as a monotherapy for MS prevention.

Keywords: Multiple Sclerosis, Vitamin D

The bioinformatic approach reveals the SNP-mediated lncRNA NONHSAT017462.2 and hsa-miR-6887-3P interaction with the potential impact on the ESCC risk (Research Paper)

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Introduction: Esophageal cancer is the sixth leading cause of death from cancer and one of the most minor studied cancers worldwide. This study's objective was to explore the regulatory network constituted by long noncoding RNA (lncRNA), miRNA, and mRNA (MMP-9) in ESCC.

Methods: We evaluated the significance of gene expression in ESCC by analyzing raw data from the Gene Expression Omnibus (GEO) database with GEO2R and also we used DAVID, KEGG pathway, miRWalkv.3, and Venn diagram. Eventually, we illustrate the effective SNP between lncRNA-miRNA with the LncRNASNP2 database.

Results: We chose gene expression datasets of GSE161533 from the GEO database to find out a fundamental gene and their interaction network during the progression and metastasis of ESCC. Matrix metalloproteinase-9 (MMP-9) separately extracted to undertake KEGG pathway (cancer signaling pathway)enrichment analysis using DAVID. We used miRWalkv.3 and LncRNASNP2 online databases to search for the targets of gene miRNAs. To summarize, we compared the overlap between two lists of miRNA identifiers by using area-proportional Venn diagrams. Using the LncRNASNP2 database, we found the SNP rs763141577 in hsa-miR-6887-3P target sites on lncRNA NONHSAT017462.2 influence the miRNAâ€"lncRNA interactions, thereby alter their functions. These findings allow us to infer that it is the changes of the related functions and pathways that caused the tumorigenesis of ESCC

Conclusion: The study demonstrates that SNP rs763141577(T/C) in lncRNA NONHSAT017462.2SNP provides an alternate binding site for microRNA

hsa-miR-6887-3p which affects the overexpression of the MMP-9 gene plays an important role in esophageal cancer metastasis.

Keywords: esophageal squamous cell cancer, MMP-9, lncRNASNP2, SNP, lncRNA, hsa-miR-6887-3P0

The effect of biological dressing on wound healing (Research Paper)

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Introduction: Basically, in the treatment of burns, the time of hospitalization, the amount of money spent on treatment, the amount of manpower used, and the creation of minimal complications after recovery are the points that should be used in burns of limbs, especially hands and feet. Be of special importance. This study is a clinical trial that has studied the effect of a treatment method (biological dressing using amniotic fluid) on the healing process, infection rate and pain intensity of burn wounds.

Methods: In this study, 80 patients with grade 2 deep burns in non-axial limbs were studied. Samples were selected by Poisson sampling method. The procedure was performed in such a way that the amniotic fluid was obtained from the placenta of women who had undergone cesarean section and after performing hepatitis B, AIDS, sepsis and culture tests, it was placed on the wounds of patients who had the characteristics of the study units. During different days, the condition of the wound in terms of healing and severity of pain was checked with a checklist related to pain, and in case of possible symptoms of wound infection, blood culture and wound discharge were performed simultaneously and the incidence of infection was assessed.

Results: The mean time of complete healing of burn wound in the studied units was 12.03 days. While in other statistics, the healing time of half-thickness burn wounds is more than 3 weeks. The incidence of infection in the studied patients was 2.5%, which contained infection with Pseudomonas aeruginosa, while in the presented statistics, there was 9% infection with Pseudomonas. There is also pain reduction in the units under study.

Conclusion: The results of the study showed that the use of biological dressing (amniotic fluid) in second degree burn wounds reduced the rate of infection (2.5%), accelerated wound healing and reduced the need for analgesic due to the amniotic adhesion to the wound and the closure of the terminal Are nervous.

Keywords: Biological dressing, extensive burns, healing

The effect of the Mediterranean diet on reducing the risk of prostate cancer (Review)

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Introduction: Introduction: Mediterranean diet (MD) due to its anti-inflammatory, anti-fat and chemical properties may be beneficial for men with localized prostate cancer (PCa) under active supervision (AS). This study prospectively examines MD adherence to Gleason score progression and examines the association with diabetes status, statin use, and other factors. The aim of this study was to evaluate the effect of Mediterranean diet on reducing the risk of prostate cancer.

Methods: Methods: This study was conducted in 1399 by searching for keywords such as diet, Mediterranean diet, growth risk, cancer and prostate in reputable databases such as: pub med and google scholar. Finally, 15 articles were found, of which 15 articles 10 articles were used

Results: Results: Based on studies from articles, the results show that in one study, researchers at the University of Texas found that those on a Mediterranean-like diet experienced a better course of illness. This study, taking into account factors such as age, prostate-specific antigen (PSA) and tumor size, concluded that people on a diet high in fruits, vegetables, legumes, whole grains and fish reach a stage of the disease that requires active treatment. Have. The researchers also found that diabetes and the use of statins were associated with a reduced risk of developing prostate cancer. The Mediterranean diet was more effective in non-white people. This is important because, for example, in the United States, blacks are more likely to develop the disease and have more adverse outcomes.

Conclusion: Conclusion: According to the findings, it is better to set up a program to reduce the risk that the risk factor is not dangerous for us and it is recommended that we continue to do the treatment process and proper protection to do a good job of this study.

Keywords: Diet, Mediterranean, risk of growth, cancer and prostate

The effects of Candida albicans isolated from human feces and standard Lactobacillus plantarum on colorectal cancer (Research Paper)

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Introduction: In recent studies, Probiotics have been shown to mediate anti-cancer effects through the immune system. The aim of this study was to investigate the effects of Lactobacillus plantarum and Candida albicans on the process of colorectal cancer caused by fatty foods and azoxymethane in rats.

Methods: Male Fisher 344 rats were divided into 6 groups of 5. One group received fatty foods with liquid oil and the other group received fatty foods and azoxymethane. The third group received only azoxymethane and after proving cancer, the groups were treated separately with Lactobacillus plantarum standard, Candida albicans isolated from the elderly's gastrointestinal tract, and a chemotherapy drug. Candida albicans isolated from human feces were evaluated by biochemical, microbiological, and PCR methods. After treatment of the groups, the serum levels of IFN-Î³, IL-4 and TGF-Î², and TNF-Î± were measured by ELISA, and the intestinal tissues of rats were examined pathologically.

Results: The results showed that cancer cells in groups treated with chemotherapy and microorganisms developed apoptosis, which was characterized by shrinkage and darkening of cell nuclei. Serum levels of IFN-Î³, IL-4, and TGF-Î² significantly decreased compared to the control group ($P<0.05$).

Conclusion: Microorganisms of the microbial flora of the gastrointestinal tract of the elderly and healthy people play an effective role in improving gastrointestinal diseases because their probiotic properties are effective in controlling and preventing diseases.

Keywords: Colorectal cancer, IFN-Î³, IL-4, TGF-Î², TNF-Î±

The mechanism of drug delivery and engineering of antibodies in cancer targeted therapy Challenges and Benefits (Review)

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Introduction: Cancer is one of the most challenging diseases and a significant cause of death in the world. Recently, cancer has been considered as one of the leading causes of death worldwide and much research has been done to overcome this public health problem. Although much effort has been made to design new chemotherapy drugs, only some of which have shown significant effects on cancer cell destruction, the inability of these drugs to distinguish between healthy and cancer cells leads to systemic toxicity and adverse side effects. Be. Also, resistance to chemotherapy is another problem with successful tumor control. To date, immunotherapy has been considered the most promising treatment for systemic cancer, compared to conventional anticancer strategies. Administration of cytokines, immunosuppressants, and monoclonal antibodies to tumor-targeting (mAbs). In this review, we will discuss drug delivery potentials, which include a range of methods to enhance immunotherapy.

Methods: In this study of drug delivery potentials, we used Google Scholar, Pubmed, and Online Wiley databases to enhance the safety of drugs.

Results: In addition to these benefits, however, serious toxicities characterize a wide range of immune-modulating drugs. Thus, a challenge in this area is to develop effective strategies to curb the potential of combination therapies while preventing the debilitating toxicities that prevent immune therapies from reaching their full therapeutic potential.

Conclusion: Targeting toxic compounds to tumors has historically been pursued as a strategy to increase the efficacy and limit the systemic toxicity of cancer therapies. To this end, much effort has been made to produce nanoparticles that passively amplify the accumulation of small molecule chemotherapies and targeted drugs in tumors.

Keywords: Cancer treatment, Antibody Monoclonal, Resistance to chemotherapy, nanoparticles

The place of individual genetics in susceptibility to COVID-19 (Review)

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Introduction: Covid19 has recently spread widely as a complex disease and epidemic around the world. Although most people with the disease are elderly or have major medical problems such as cardiovascular disease, high blood pressure, diabetes, or cancer, some of the victims are healthy and even relatively young and in different age groups. The sequence of patients' genomes for disease-related DNA alterations helps explain this mystery. Genetic changes in genes related to immune function, including human leukocyte antigen (HLA), are emerging as an important determinant of Covid19 infection. One of the ways the SARS-COV-2 virus enters the ACE2 receptor, Therefore, the genetic variants of the ACE2 receptor can be another important factor in the genetic susceptibility to Covid19.

Methods: In this review study, searches were performed in the electronic and scientific databases of PubMed, Medline, Google Scholar, Scopus, and ISI, and valid articles related to the subject were searched using the keywords genetics, immunology, and COVID-19.

Results: The results of studying genetic findings in different communities and the susceptibility of people to this disease will be an important step to help personal and predictive medicine.

Conclusion: The purpose of this study is to show the place of individual genetics in susceptibility to COVID-19, which requires extensive and more research in this field and allows researchers and physicians to use the information obtained to manufacture effective drugs and vaccines.

Keywords: Genetics, Immunology, Covid19, Personal medicine

The potential of Whartonâ€™s jelly in regenerative medicine applications (Review)

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Introduction: Wharton's jelly is a gelatinous substance within the umbilical cord with highlight applications for regenerative medicine. Wharton's jelly is rich of extracellular matrix (ECM) components and acts as a mucous connective tissue containing some fibroblasts, macrophages, and also mesenchymal stem cells (MSCs) as well as exosomes. Moreover, because it is a waste of childbirth without ethical issues, it could be an appropriate source for regenerative medicine applications. In this review,the three major advantages of Wharton's jelly for regenerative medicine are introduced. ECM components of Wharton's jelly include mucopolysaccharides such as hyaluronic acid and glycosaminoglycans (GAGs), and also proteins such as collagens and peptide growth factors. An appropriate scaffold for tissue engineering should simulate the structure of the natural ECM to facilitate cell adhesion and proliferation. Natural biomaterials for scaffold fabrication are functionally superior to synthetic ones due to providing a microenvironment resembling the natural ECM and biological cues, which provide superior cell attachment, proliferation, and differentiation. Recently, decellularized ECM has paied many attentions in the ï¬eld of tissue engineering. After decellularization, the xenogeneic and allogenic antigens are removed while retaining the ECM components. Besides, Wharton's jelly contains primitive mesenchymal stem cells (MSC) with the highest concentration per millilitre than other allogeneic tissues. Whartonâ€™s jelly MSC may be more effective than MSC from adult tissues in the treatment of several conditions, and though safe and efficient. Exosomes are a type of extracellular vesicles with a diameter ranging from ~ 30 to 150 nm, derived from a sequential process of multivesicular body membrane remodelling. Exosomes could be found in multiple body fluids, such as blood plasma, amniotic fluid, and Whartonâ€™s jelly. Exosomes are secreted from several cell types, especially stem cells and play a significant role in intercellular communications. Recently, exosomes have also emerged as an attractive cell-free therapeutic alternative with great regenerative potential.

Methods: -

Results: -

Conclusion: In conclusion, Wharton's jelly could introduced as a significant source for regenerative medicine due to: 1) high amounts of ECM components which can use as scaffold constructs for better cell adhesion, proliferation and differentiation, 2) MSCs which are more safe and efficient than other multipotent stem cells, and 3) exosomes which currently consider for cell-free therapies to avoid the limitations of cell therapy.

Keywords: Wharton's jelly, ECM, MSCs, Exosome

The relation between VEGF therapies and diabetic retinopathy (Review)

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Introduction: Diabetic retinopathy is a major public health and economical burden worldwide. Clinical findings and surgical results showed the use of antivascular endothelial growth factor (VEGF) agents (anti-VEGFs) for treating diabetic retinopathy (VEGF is one of the important survival factors for endothelial cell). Risk factors and anatomical or functional success in recent years proved effect of anti-VEGFs on diabetic retinopathy.

Methods: As we searched we find out 423 article about this topic. 49 articles were not in English and68 of them did not have enough evidence for their studies. Also 56 were not updated and did not have fresh results.215 of them were related to our study and among those, 35 had useful and new information. Thus we utilized articles that were beneficial.

Results: VEGF plays pivotal role in the development of diabetic retinopathy. Based on experiments and investigations,Serum levels of VEGF were detected by ELISA were significantly high in patients with diabetic retinopathy. In addition, gap junction-dependent intercellular communication in various nonretinal vascular cells can be inhibited by VEGF. Furthermore, VEGF was expressed in the vessels of fibrovascular membrance (FVMs) marked with anti-CD34 antibody (recognized as a microvascular endothelial cell marker). This suggested that VEGF was involved in angiogenesis and contributed to the formation of FVM in diabetic retinopathy progress. To supporting the importance of posttranscriptional mechanisms; the increased abundance of VEGF protein expression in response to diabetes was observed in the absence of a change in VEGF mRNA expression. As a result, the patients that were in process of studies, presented a very good response to the treatment. Already after first anti-VEGF intravitreal injection the substantial decrease in central retinal thickness was to observe.

Conclusion: It could be explained by the fact, that VEGF is a secreted protein and loss of VEGF produced by a single cell-type can be compensated by others. Additionally, Delineating detailed mechanisms provided that the presence of at least seven VEGF receptors and coreceptors accounts for the difficulties in revealing their mechanisms.

Consequently, Several lines of evidence point that VEGF act as a key regulator of diabetic retinopathy and provide a potential tool for risk assessment in diabetic patients.

Keywords: Diabetic retinopathy-Vascular Endothelial Growth Factor

Type 2 diabetes prediction based on genetic polymorphisms (Review)

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Introduction: Diabetes mellitus is one of the most prevalent diseases and is expanding significantly. Approximately half a billion people living with diabetes around the world, and 212 million individuals have been undiagnosed. (1) Diabetes mellitus classified into three major types: type 1 diabetes, Type 2 diabetes, and gestational diabetes. Type 2 diabetes is a complex disease that occurs in a complex interplay of genetic and environmental factors. (2) In general, diabetes is likely to be controlled effectively, and complications can be avoided when diagnosed early. As the risk of getting the disease is influenced by heredity, early diagnosis and effective diagnostic recommendations become possible. For the sake of the role of genetics in the prediction of type 2 diabetes, we will propose to predict type 2 diabetes mellitus using genetic polymorphisms. We identify and compare the most recent GWAS(genome-wide association study) studies to select the genetic polymorphisms, which can be applied for the prediction of type 2 diabetes.

Methods: The databases for the literature search were chosen, based on a recommendation of the optimal database combinations. (3) As for the literature search, the three chosen databases were Scopus, Web of Science, and PubMed. The databases searched for studies of GWAS for T2D, published between 2000 and September 2020. According to these article results, the related type 2 diabetes polymorphisms were chosen, proven in at least three GWAS studies.

Results: There were a total of 63 articles collected from PubMed, Scopus, and Web of Science. After removing the duplicates, the total number of studies obtained was 26. As to the previously mentioned criteria, five polymorphisms, which at least three GWAS studies revealed their association with type 2 diabetes, were selected. Afterward, given the OR (odds ratio) of these polymorphisms, the feasibility of type 2 diabetes was evaluated. These polymorphisms are: rs10830963(4,5), rs1801282(6), rs13266634(7), rs7903146(7) and rs4402960(8).

Conclusion: GWAS are powerful tools to support the diagnosis, and they could be an effective tool to predict the risk of pre-symptomatic diabetes. Usage of GWAS studies and their results could pave the way for devising meticulous methods to determine the feasibility of various diseases, including type 2 Diabetes. Above all, a wide range of complementary scrutiny is required to boost the effectiveness of these methods.

Keywords: diabetes, type 2 of diabetes, GWAS, polymorphisms

Understanding of hsa-miR-221-3p role in Prostate Cancer process by bioinformatics analysis (Research Paper)

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Introduction: These days, Prostate Cancer (PCa) is one of the leading causes of cancer death for male. Recent studies shown that the development risk of PCa can be a genetic factor or inherited. According to the researches miRNAs (small non-coding RNAs) and SNPs (single nucleotide polymorphisms) might develop the progression of Prostate Cancer. A large scale studies of researches lead us to hsa-mir-221-3p chromosome X for bioinformatics analysis of Prostate Cancer.

Methods: Bioinformatics analysis of this study have been done by using miRBase , miRTarbase , miRWalk , TargetScan , DIANA TOOLS , DAVID ,miRdSNP ,Gene MANIA , HeatMAP , miRNASNP databases, GraphPad Prsim 8.0 and R ,a programming language, were needed to get required data about mircoRNA basis , validated and predicted target genes , gene's expressions , signaling pathways , SNP and genes' interaction .

Results: Based on hsa-mir-221-3p target genes, BCL2, CREB1, MMP3 and MDM2 are considered as the most frequent genes of Focal adhesion, MAPK, TNF and proteoglycans in cancer signaling pathways, that all show the same pattern in Prostate Cancer. Moreover, in the bioinformatics analysis of this study, the occurrence of rs3737336 in CDON, a target gene, might have impact on Prostate Cancer progression, which in order to discover the exact role of this SNP in Prostate Cancer, the further analysis is needed.

Conclusion: Analysis of Focal adhesion, MAPK, TNF and proteoglycans in cancer signaling pathways, showed apoptosis, genomic instability, invasion and cellular migration processes in Prostate Cancer via the activation of BCL2, CREB1, MMP3 and MDM2 which they are activated by a cascade of genes. Thus, the function prevention of the mentioned genes results in suppression of the pathways and noted the tumor suppressor role of hsa-mir-221-3p in Prostate Cancer process. For the better understating of hsa-

mir-221-3p role in Prostate Cancer, the investigation of role in this cancer, rs3737336 is needed.

Keywords: Bioinformatics, miRNA, SNP, PCa, Signaling pathways

Understanding of hsa-mir-654-3p role in Lung Cancer process by bioinformatics analysis (Research Paper)

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Introduction: Lung Cancer is the leading cause of years of life lost because of cancer and is associated with the highest economic burden relative to other tumor types. Early diagnosis and treatment has a significant role in the progression and development of cancer. There are many different factors in the prevention, diagnosis and treatment of Lung cancer. Recently, it has been shown that small non-coding RNAs like Micro-RNAs can be used to treat or diagnose various diseases. Therefore, in this bioinformatics study has been used enrichment analysis method to evaluated the role of hsa-mir-654-3p in Lung Cancer. Survey the genome's variation has direct relationship with identifying and diagnosing different types of cancer. By controlling the gene expression, micro-RNAs can play an important role in inhibition of cancers. Consequently, the occurrence of various mutations can lead to change the efficiency of micro-RNAs action.

Methods: First, the information of hsa-miR-654-3p extracted from the miRBase database. Then, the target genes of hsa-mir-654-3p were obtained using miRTarbase, miRWalk, TargetScan and DIANA TOOLS databases, respectively. Enrichment analysis of microRNA's was done by David's database. By using GraphPad Prsim 3.8.0 , databases and R a programming language, were selected to obtain essential data about microRNA basis. Using the Genemania database, the interactions between the key genes of this study was obtained. Afterwards And then the effect of SNP on microRNA's attachment tendency, gained from miRSNPdb, miRdSNP and miRNASNP database.

Results: According to the study, it was determined that hsa-mir-654 by affecting the genes ERK, Cycline D1, K-ras, FOXO3, PKC in "MAPK signaling pathway, ErbB signaling pathway, Ras signaling pathway, PI3K-Akt, Calcium signaling pathway" may have role of Lung Cancer. Also, rs1063054 in NBN gene have recognized as a potential biomarker in Lung Cancer. Genes'

expression analysis via heatmap method, showed that K-ras gene of hsa-mir-654-3p, probably assigns the largest difference in its expression among solid tissue normal and primary solid tumor.

Conclusion: Analysis of MAPK, ErbB, Ras, PI3K-Akt and Calcium signaling pathway showed proliferation and anti apoptosis role in Lung Cancer via the activated of ERK, Cycline D1, K-ras, FOXO3, PKC genes which they are activated by a cascade of genes. Thus, the function prevention of mentioned genes results oncogenic role of hsa-mir-654-3p in Lung Cancer. For a better understanding of the hsa-mir-654-3p role in Lung Cancer, the investigation of rs1063054 role in this cancer, is needed.

Keywords: Bioinformatics, miRNA, SNP, Lung Cancer, Signaling pathways

Use of a consortium of halophilic bacteria isolated from the Salt Lake of Howz-E Soltan of Iran to increase the efficiency of Hydrolysis enzymes (Research Paper)

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Introduction: Hypersaline lakes, with salinity, ranges at or near saturation are extreme environments; yet, they often maintain remarkably high microbial cell densities and are biologically very productive ecosystems. To adapt to saline conditions, bacteria have developed various strategies to maintain cell structure and function. Studies of such bacteria are of great importance, as they may produce compounds of industrial interest, such as extracellular, hydrolytic enzymes that have diverse potential usage in biomedical science and chemical industries. Halophiles are an excellent source of such enzymes which are not only salt-tolerant, but also may be active at high temperature and pH values.

Methods: Bacteria were isolated from the hypersaline site, in a solid medium supplemented with various salt concentrations ranging from 1 to 20 g/L. Physical and chemical characteristics of samples from the isolation site were determined to suggest eventual correlations with the occurrence of the halophilic bacteria. Assays on enzymatic activities were performed in submerged cultures in the presence of various salt concentrations and appropriate substrates.

Results: As a result, the growth of the strains in the medium containing 1to20% (w/v) NaCl determined that the majority of the isolates were moderately halophile. The results represented that H2-5 and H2-6, have CMCase activity and increase together as a consortium. The bacteria cultures for evaluated for their antibiogram for diversity between halophiles and archaebacteria and it has shown that they are halophiles. Phylogenic tree analysis also showed that two strains of H2-5 and H2-6 belong to Metabacillus halosaccharovorans.

Conclusion: Together, these two isolates showed high hydrolytic activity relative to separate activity and had good results, and the two, which are highly halophilic, have excellent biotechnological applications due to their ability to produce different hydrolysis. Highly halophilic bacteria showed higher potential for the production of consortium enzymes compared to moderate halophiles.

Keywords: Halophiles, Hydrolysis, Isolation, Consortium

Use of metabolic engineering in inhibiting the cellular metabolism of lactic acid bacteria (Review)

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Introduction: Using metabolic engineering, new biosynthetic metabolic pathways can be created in important industrial microorganisms for the production of biofuels, biomaterials and other applications. Lactic acid bacteria, in addition to their major role in the fermented food industry to produce metabolites that affect the aroma, taste, stability, shelf life and texture of fermented foods, have the ability to produce valuable industrial metabolites that have potential applications in various industries, including waste processing. These bacteria are one of the selected bacteria to produce valuable industrial metabolites due to their specific genetic structure and regulatory control of their central metabolism.

Methods: In recent years, with advances in metabolic engineering strategies, genetic manipulation and regulation of cellular metabolism have been successfully performed in various laboratory disciplines because lactic acid bacteria have a strong and highly efficient expression system. These capabilities also provide the basis for the industrial competition of these bacteria. Despite the fact that metabolic engineering has great potential to improve the cellular characteristics of the microorganism, the implementation of metabolic engineering strategies to develop high-performance plants that face economic challenges for industrial-scale production is still empirically challenging. The direct concern of metabolic engineering is to understand the nature, flux distribution, and regulatory mechanism of metabolic pathways associated with a microorganism.

Results: Genome-scale metabolic modelling has now been successfully used to reconstruct efficient metabolic networks and optimize flux. Also, hybrid approaches focus on hybrid system engineering and genome-scale metabolic deletion that can help create new products and enzymes with improved catalytic properties and higher expression levels. Therefore, this review provides a brief overview of the existing metabolic engineering strategies for the comprehensive regulation of lactic acid bacterial strains

for the production of important large-scale industrial metabolites that take steps to improve this method.

Conclusion: Another major experimental challenge to performing metabolic engineering is the integration of genes encoding enzymes with diverse evolutionary and physiological histories to construct new/non-new natural pathways. Therefore, sometimes this prevents the regulation and kinetics of the relevant path, which ultimately limits the performance of new or artificial paths. However, to further expand the range and applications of this bacterium, powerful and multiple genomic manipulation tools are needed to produce cost-effective, large-scale, valuable metabolites in the laboratory.

Keywords: Metabolic engineering, Cellular metabolism, Lactic acid bacteria

Vitamin C in the formulation of inactivated COVID-19 vaccine candidate induced Th1 pattern in the aged mice. (Research Paper)

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Introduction: The morality rate of COVID-19 elevated in elderly people by 22%. Moreover, according to the reports, 90% and 80% of death in patients aged 60 years and 70 years have recorded. Aging is physiologically accompanied by a reduction in the function of the immune system, which there is a relationship between alteration in the immune system and susceptibility to infections. IFN-Î³ has a crucial role in the defense against viruses. Since the production of IFN-Î³ declines in older adults. It may explain the reason of the susceptibility of the elderly to viral infectious diseases such as COVID-19. Studies show the potency of vitamin C in the improvement of immune responses of aged people. Here, we formulated inactivated COVID-19 vaccine in vitamin C and the potency of vaccine assessed in the aged and young mice.

Methods: A SARS-CoV-2 strain was isolated from a patient and propagated in Vero cell line. The virus was inactivated using formalin and purified using column chromatography method and then quantified by Bradford. In order to formulate in Alum-based vaccine, 2Âµg of inactivated COVID-19 virus in PBS buffer was admixed with 200Âµg of Alum hydroxide adjuvant (for each dose of vaccine formulation) and shaked at 100 RPM for 60 minutes at room temperature and allowed that the viral particles to adsorb on the surface of Alum gel. And then vitamin C at concentration of 1 and

10mg/dose was added to the vaccine formulation. Young (6-8-week-old, N=32) and aged (16-20-month-old, N=32) male C57bl/6 mice were purchased from Pasteur Institute of Iran and grouped as below; Group 1: Aged mice immunized with inactivated COVID-19-Alum. Group 2: Aged mice immunized with inactivated COVID-19-Alum with1 mg vitamin C. Group 3: Aged mice immunized with inactivated COVID-19-Alum with10 mg vitamin C. Group 4: Aged mice immunized with PBS. Group 5: Young mice immunized with inactivated COVID-19-Alum. Group 6: Young mice immunized with inactivated COVID-19-Alum with1mg vitamin C. Group 7: Young mice immunized with inactivated COVID-19-Alum with10mg vitamin C. Group 8: Young mice immunized with PBS. Experimental mice were immunized with 2Âµg of inactivated COVID-19 formulated vaccines subcutaneously on days 0 and 14 and two weeks after last shot IFN-Î³ and IL-4 cytokine were assessed with ELISA and specific IgG titer, IgG1/IgG2a isotypes determined with ELISA. **Results:** The results of IFN-Î³ and IL-4 cytokines in experimental groups demonstrated that injection of COVID-19 vaccine formulated with vitamin C in young and aged mice shows a significant increase as compared with the control and mere vaccine groups (P< 0.0401). In addition, specific total IgG and IgG1/IgG2a level improved in young and aged mice.

Conclusion: It seems that vitamin C is useful in the improvement of specific immune responses against COVID-19 vaccine in young and aged people.

Keywords: COVID-19 vaccine, vitamin C, Adjuvant, aging

Waste Recycling, Extraction of Dirty Gold (Research Paper)

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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