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1. A brief history of circular RNAs (CircRNAs) (Review)

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Introduction: The concept of circular RNAs (circRNAs) was first proposed in 1976 by Sanger et al. They attempted to understand how viroids act as plant pathogens. They studied four diverse purified viroids and explained that RNA molecules in viroids are unable to be labeled at the ends of 5Õœ and 3Õœ and they tolled viroids are covalently connected circular RNA molecules. CircRNAs were discovered in mammals in 1991. Comprehensive research on circRNAs started with the discovery of large amounts of circRNAs in human cells in 2012. Compared with conventional linear RNA, the end of 5Õœ-3Õœ in circRNAs are covalently closed, so circRNAs, in order to maintain stability, do not need a cap and poly-A tail at their 5Õœ and 3Õœ ends. CircRNAs have higher stability, especially against degradation of exonucleases, which is a structural advantage for them. CircRNAs are found in all branches of life, for example as the genome of viroid plant pathogens and hepatitis delta virus (HDV) or appear as rRNA introns, spliced tRNAs, and mediators of rRNA processing in the archaea. In addition, circRNAs are found within the life cycle of group I eukaryotic and bacterial introns. CircRNAs are categorized as exonic (ecircRNA), exon-intron (EIcircRNA), or intronic (ciRNA). CircRNAs may stay within the nucleus or enter the cytoplasm. CircRNAs make it possible to replicate within the form of a rolling circle. Although most circRNAs contain exons of protein-coding genes, circRNAs can also originate from introns, intergenic regions, UTRs, ncRNA loci, and antisense sites with known transcripts.

Methods: This study has performed by searching the â€œPubMed databaseâ€□ and â€œGoogle scholarâ€□ by different combinations of terms â€œcircRNAâ€□ and â€œhistory of circular RNAsâ€□. The concept of the RNA circle was investigated.

Results: Studies have shown that the aberrant expression of cyclic RNA plays a vital role in the progression of various human diseases. RNA circles represent a powerful tool in future biotechnology and gene transfer research for the development of new gene therapies.

Conclusion: CircRNAs have great potential and there is still a lot of unknown about circRNAs. With the persistent efforts in this field, circRNAs will play a basic role in research and medical applications and become an important part of human health shortly.

Keywords: CircRNA, Circular RNA, RNA synthesis, Splicing.

A careful scrutiny of the HES1 gene regulation in glioblastoma tumorigenesis (Research Paper)

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Introduction: Glioblastoma (GBM) is a grade 4 glioma brain tumor arising from brain cells called glial cells. The current standard glioblastoma multiforme treatment has resulted in more people living two, three or four years. Although advances have been made in the treatment of GBM, due to rapid necrosis and abundant angiogenesis, GBM is still deadly. Patients diagnosed with these tumors usually see a doctor with severe symptoms and poor quality of life. The goal of this study is investigating the HES1 (Hes Family BHLH Transcription Factor 1) gene as a major actor with a vague role in glioblastoma, and find its communication with a lncRNA and a miRNA, using bioinformatics data.

Methods: To begin, HES1 gene was structurally analyzed in GeneCards, then HES1-related single nucleotide polymorphisms (SNPs) and microRNAs were found in miRdSNP and NCBI databases. In another part of the project, the LncRNADisease database (version 2.0) helped analyze data to find a long non-coding RNA (lncRNA) interconnection with the HES1 gene signaling pathways.

Results: HES1 gene is a Protein Coding gene and located on chromosome 3q29. According to findings from the GEPIA2 database, the HES1 gene is highly expressed in glioblastoma. The analysis showed that the occurrence of the SNP:rs11541817 can lead the cells to glioblastoma and affect the involved miRNA-23a in this process. Through the process of this disease, the disease-associated SNP (rs11541817) is located on the mRNA and causes the disease. When miRNA-23a binds to 3â€™UTR of HES1 mRNA, it increases gene expression and intensifies the tumorigenesis of GBM. On the other hand, lncRNA-ZFAS1 as a prognostic factor by activating of the Notch signaling pathway, promotes glioblastoma cell progression because Notch, leads the HES1 gene to overexpression.

Conclusion: Based on these observes, it is inferred that the interaction of lnc-ZFAS1 with Notch signaling pathway could be useful biomarker for the diagnosis of glioblastoma. Furthermore, the miRNA-23a prove that HES1 is an effective gene in GBM outbreak and its tumorigenesis.

Keywords: Key Words: HES1 gene, glioblastoma, rs11541817, miRNA-23a, lncRNA-ZFAS1

A network-based approach to identify hub genes and key pathways in esophageal squamous cell carcinoma (Research Paper)

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Introduction: Esophageal cancer is the sixth leading cause of cancer death worldwide (1). The most common type of esophageal cancer is esophageal squamous cell carcinoma (ESCC), with high mortality (2). Screening this cancer using biomarkers in endemic areas with high-risk populations can reduce the mortality from this disease worldwide. Gene expression profiling using microarray technology and the combination of resultant data with in silico approaches can provide valuable information about differentially expressed genes in cancer and normal cells (3, 4). Since several databases collect and maintain microarray data, we can analyze the gene expression profile of different cancer for different goals. This study was designed to discover hub genes and pathways which are enriched with differentially expressed genes in esophageal squamous cell carcinoma.

Methods: A gene expression profile of esophageal squamous cell carcinoma (GSE75241) was obtained from gene expression omnibus (GEO) available at https://www.ncbi.nlm.nih.gov/geo. There are 15 tumor samples and 15 nonmalignant samples in the selected dataset. GEO2R was used to identify differentially expressed genes (DEGs) between tumor and normal samples. Genes with p-value < 0.05 and log fold change (logFC) > 1 and -1 < were considered as final DEGs. Up-regulated genes were used for further analysis. Enrichr (https://maayanlab.cloud/Enrichr) was exploited for enrichment analysis. Therefore, using Enrichr gene ontology (GO) term and Kyoto encyclopedia of genes and genomes (KEGG) pathway enrichment analysis were conducted. Moreover, STRING (https://string-db.org/) was used for protein-protein interaction (PPI) network reconstruction and Cytoscape 3.9.0 was employed to visualize and analyze PPI-network. Using the CytoHubba plugin and degree centrality top 10 hub genes were selected. Ultimately, hub gene validation was performed using UALCAN available at http://ualcan.path.uab.edu/index.html.

Results: Based on the selected criteria, 868 genes were up-regulated and 628 genes were down-regulated. Considering GO biological process, up-regulated DEGs are associated with â€œextracellular matrix organizationâ€• , â€œextracellular structure organizationâ€□, and â€œexternal encapsulating structure organizationâ€• . GO Molecular function revealed the relationship of up-regulated DEGs with â€œsingle-stranded DNA helicase activityâ€• , â€œchemokine activityâ€□, and â€œprotease bindingâ€□. GO cellular

components showed that up-regulated DEGs are related to â€œcollagen-containing extracellular matrixâ€□, â€œendoplasmic reticulum lumenâ€• , and â€œfocal adhesionâ€• . KEGG pathway enrichment analysis showed the relationship of up-regulated DEGs with â€œECM-receptor interactionâ€• , â€œFocal adhesionâ€□, and â€œAGE-RAGE signaling pathway in diabetic complicationsâ€• . PPI-network was reconstructed using STRING. The reconstructed network of up-regulated DEGs consisted of 823 nodes and 11269 edges. Based on degree, FN1, IL6, IL1B, CCNB1, PTPRC, CDK1, MMP9, BRCA1, TLR4, and MKI67 were considered as hub genes. UALCAN showed that among selected hub genes, only two genes (IL6 and IL1B) have a reverse relationship with the survival of esophageal carcinoma patients.

Conclusion: Using an integrated network-based approach with microarray data our results revealed top pathways and biological components related to DEGs in esophageal squamous cell carcinoma. Moreover, we suggest two validated hub genes (IL6 and IL1B) as potential biomarkers in esophageal squamous cell carcinoma.

Keywords: Esophageal cancer- esophageal squamous cell carcinoma (ESCC) -microarray

A new mechanism in potassium channel blockage identified for a scorpion venom peptide (Research Paper)

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Introduction: Scorpion venom is a source of ion channel modifier peptides with interesting pharmacological properties. Here, in addition to reporting the structure of a peptide(meuK2-2), identified in the Mesobuthus eupeus venom gland, its interaction with Kv1.3 channel was also interpreted.

Methods: Three-dimensional structure of meuK2-2 was generated using MODELLER and I-TASSER,PHYRE2,Robetta servers. The best model was selected according to Z-score;and considered for further optimization using MD simulation.Interaction of meuK2-2 with the Kv1.3 channel was also evaluated using peptide-protein docking experiments with HADDOCK software, subsequently pose clustering and also, 100 ns MD simulations using a protein-water system in the NVT ensemble by Gromacs to evaluate the binding interaction between meuK2-2 and Kv1.3.The final docked complexes were then subject to minimization with CHARMM force field and investigated key interacting residues, electrostatic interactions, binding free energies, folding pattern, hydrogen bond formation, hydrophobic contacts.

Results: 3-D structure of the meuK2-2 is composed of a cysteine-stabilized Î±-helical and Î²-sheet(CSÎ±/Î²) folding.Two key residues and H-bonds are involved in the binding of meuK2-2 to Kv1.3.In a new mechanism meuK2-2 binds to both turret and pore loop of the channel.The binding of meuK2-2 induces some conformational changes to Kv1.3. This is followed by occupation of the pore of the channel with the side chain of a His9 residue.Altogether blocks the ion permeation pathway.

Conclusion: A new mechanism was predicted for channel blocking with meuK2-2.Since Kv1.3 plays a significant role in human T cell activation, meuK2-2 have a potential for further investigations to develop as a pharmacological tool in treatment of autoimmune diseases.

Keywords: Mesobuthus eupeus; Venominvformatics; Potassium channel blocker; Homology modeling; Natural peptide

A review on COVID-19 mRNA vaccine candidates in clinical trials: design, target and formulation strategies (Review)

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Introduction: Ongoing Coronavirus disease 2019(COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus -2(SARS-CoV-2) has impressively affected many dimensions of human lives and results in millions of infections and deaths worldwide. There is no recognized treatment for COVID-19 and Vaccination has been introduced as the last hope to stop the pandemic. Various vaccine platforms have been used for COVID-19 vaccine development. Among them, mRNA vaccines belong to Pfizer/BioNTech and Moderna companies demonstrated both high efficacy and safety and were the pioneers to receive FDA full approval. This transformative technology has unique advantages over other vaccine platforms. mRNA vaccines are Rapidly designed and produced through a simple manufacturing process. They can induce both potent humoral and cellular responses and importantly are safer than DNA vaccines. Of note, this platform is versatile to design novel variant-specific vaccines so is the best vaccine technology for emerging viruses such as SARS-CoV-2 and influenza. Importantly, recent improvements in the field of stability and delivery spot more light on this technology. These improvements include the efficient delivery of mRNA by lipid nanoparticles(LNPs) delivery system and, the utilization of modified nucleotides to enhance protein production and avoidance of excessive innate immune activation. There are also other COVID-19 mRNA vaccines in preclinical and clinical trials with promising results which are developed in order to respond to the current requirement for more efficient vaccines to control the pandemic. Approximately, most COVID-19 mRNA vaccines are used prefusion stabilized spike protein as the target antigen. Spike protein is placed on the virus envelope, composed of S1 and S2 subunits, and mediates the virus entry into the host cells through the interaction of receptor-binding domain(RBD) of S1 subunit with angiotensin-converting enzyme-2(ACE2) receptor on the host cell surface. Further proteolytic cleavage of spike protein into the S1 and S2 domains caused the virus envelop and cell membrane fusion and viral entry. Two proline substitutions in the spike protein(S-2P) stabilize it in the prefusion state which further enhances the stability and immunogenicity. Here, we comprehensively describe different COVID-19 mRNA vaccine candidates in clinical trials. We explain each vaccine design, target, and important results. Finally, we discuss the most important future prospects and describe some strategies to develop more efficient COVID-19 mRNA vaccines.

Methods: This current review has been done by searching for original articles of COVID-19 mRNA vaccines in clinical trials in PubMed, Web of Science, and Scopus databases.

Results: The recent approval of two mRNA vaccines, BNT162b2 and mRNA-1273, and their impressive success, encouraged scientists to develop more COVID-19 mRNA vaccine candidates with different designs and targets. Collectively 5 vaccine candidates are in clinical trials. Two candidates are based on self-amplifying mRNA. One candidate, named CVnCoV, showed 48% efficacy in the phase 3 clinical trial and failed to receive approval.

Conclusion: The concept of mRNA as a new therapeutic strategy was introduced in 1989. Then mRNA drugs rapidly developed to clinical trials. During the last decades, mRNA-based vaccines have demonstrated encouraging results against infectious disease and cancer. Notably, two mRNA vaccines encapsulated in lipid-nanoparticle (LNP), BNT162b2 and mRNA-1273, have demonstrated the most promising results in the prevention of COVID-19 infection. These vaccines have shown 95% efficacy and were the first mRNA vaccines to be licensed for emergency use. Also, there are more COVID-19 mRNA vaccine candidates which rapidly developed to clinical trials and showed promising results. Despite the remarkable success of these vaccines, there remain challenges that need to be addressed. For instance, a high dosage of mRNA used in these vaccines has led to enhance production costs and caused some side effects related to LNP components. Also, novel SARS-Cov-2 variants have emerged which can escape from previously induced immunity by vaccines. Therefore, some strategies need to employ in order to develop more effective mRNA vaccines with reduced doses and costs. One potential strategy is to improve the translational efficiency of mRNA by optimization of mRNA design, 5â€™capping method, and polyadenylation approach to reduce the effective dose necessity for immunogenicity as well as side effects and costs. Another strategy to compensate for the reduced efficacy of COVID-19 mRNA vaccines is to develop SARS-CoV-2 variant-specific vaccines by employing the variant spike sequence. Collectively, more researches need to perform in order to optimize mRNA vaccines and enhance their efficacy.

Keywords: COVID-19, mRNA vaccine, SARS-CoV-2, vaccination

Acute Lymphoblastic Leukemia Treatment with CAR-T Cell Immunotherapy (Review)

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Introduction: ALL, also known as lymphocytic leukemia, is a malignancy that affects both children and adults. Malignant transformation and proliferation occur in lymphoid progenitor cells in the bone marrow, blood, and extramedullary locations. The majority of ALL cases are of the precursor B-cell type, while T-cell neoplasm is a rare and exceedingly aggressive phenotype that affects somewhat more adults than children. CAR Structures are synthetic receptors that are made up of four basic parts: an external target antigen binding domain, a hinge region, a transmembrane domain, and one or more intracellular signaling domains. Isolation of donor T cells is followed by effective activation, gene transfer of the CAR construct, CAR-T cell multiplication, phenotyping, and quality check analysis during the process of CAR-T cell therapy as an emerging treatment approach. Patients' (autologous) or healthy donors (allogeneic) peripheral blood mononuclear cells are used to make leukocytes (PBMCs). Purifying autologous antigen-presenting cells (APCs) from patients or donors, or beads coated with anti-CD3/anti-CD28 monoclonal antibodies, or anti-CD3 antibodies alone or in combination with feeder cells and growth factors, such as IL-2, are used to separate T cell subsets, which are then activated using specific antibodies.

Methods: In this study, Science Direct, Springer, Google Scholar, and PubMed content were used to evaluate the treatment of acute lymphoblastic leukemia with CAR-T cell immunotherapy.

Results: As a result, CAR T-cell therapies have several advantages over chemotherapy. Patients whose cancer recurs after numerous therapies may benefit from CAR T-cell therapy, which can help them achieve long-term remissions. Some cancer patients can go for long periods without their disease progressing. CAR T-cell therapies have a variety of advantages, including fewer infusions, a shorter treatment period, and faster recovery. CAR T-cell therapies benefit from living cells, which can multiply in the patient's body and give long-term memory. As a result, when there is a relapse, existing long-lived CAR T-cells can recognize and kill cancer cells. After a single infusion of CAR T-cell treatments, relapse patients have shown to be in complete remission for a long period. This therapy approach can be effective in removing metastatic cells in addition to treating local malignancies. Unlike the conventional adaptive immune cells, CAR-T cell treatment is a targeted therapy with great specificity that can eradicate cancer cells expressing the relevant tumor-associated antigens. As a result, this therapeutic strategy will prevent the unnecessary destruction of healthy normal cells to a large amount. CAR-T cells, surprisingly, can detect cell surface antigens without the need for MHC gene expression. By masking MHC or surface molecules involved in antigen processing and

presentation, cancer cells cannot evade the immune system (T cell immune surveillance). It's worth noting that CAR-T cells are probably certainly capable of detecting a variety of antigens, including lipids, carbohydrates, and proteins. Furthermore, chimeric antigen receptors feature a flexible intracellular signaling domain that permits the cell to prevent tumor cells from directly or indirectly downregulating costimulatory molecules.

Conclusion: Therefore, CAR T cell technology is indicated as a suitable candidate for ALL treatment as an immunotherapy-based method. As a result, this technique has a lot of promise in terms of cancer treatment. Although it faces significant obstacles such as cytotoxicity, cytokine release syndrome, neurotoxicity, and ICANS. After chemotherapy approaches fail, the development of different generations of CAR technology and its combined usage in other ways, such as hematopoietic stem cell transplantation, can be employed as an effective method of ALL treatment. Using alternate therapy strategies to address these issues appears to be critical. T cells genetically modified with Chimeric Antigen Receptor (CAR) treatment for ALL have been extensively investigated in the previous decade and represent a new era of strategy. According to the results of Phase I/II clinical trials, this technique appears to be very promising and could be employed as an effective and safe treatment for ALL soon.

Keywords: CAR T-cell, Acute lymphoblastic leukemia, immunotherapy, clinical

Advances in Platinum Nanoparticles for cancer therapy and drug delivery (Review)

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Introduction: Human mortality is caused primarily by cancer, except in cases of infectious disease. Anti-cancer drugs can be improved with nanomaterials by controlling their release and increasing their in vivo efficacy. Nanoparticles (NPs) can be used as carriers for anti-cancer drugs. Antitumor properties can be conferred by metal-based nanoparticles (mNPs), including antioxidant effects. Biomedical research increasingly uses metallic nanoparticles. It is possible to design them for both therapeutic and diagnostic purposes in the case of cancer. Nanoparticles of platinum (PtNPs) are relatively new agents being investigated for cancer treatment. Cancer therapy can be improved by using therapeutic systems based on PtNPs, which result in reduced side effects and improved efficiency. One of the most valuable approaches for treating cancer is using PtNPs as an anticancer drug. A metal-based nanoparticle can enhance the effectiveness of conventional chemotherapy by releasing anticancer agents in a targeted and controlled manner. Researchers are now focusing on how to transport drugs using PtNp-based nanoplatforms. PtNps-based nanocarriers have shown promising results in many studies, in pristine form or functionalized with targeting molecules or coated with biocompatible materials. Researchers have demonstrated that in vivo stability can be improved with such nanosystems, drugs can be accumulated in tumor sites, therapeutic effectiveness can be improved, and systemic toxicity can be reduced. It is possible to produce metallic and metal oxide nanoparticles and modify them in various ways as needed. A variety of functionalization strategies may be used to conjugate them to biological molecules (antibodies, nucleic acids, peptides), targeting ligands, and anticancer drugs.

Methods: This article is review

Results: Nanoparticles are developing rapidly and in a variety of directions, providing alternative treatment options and improving many cancer treatments. NPs based on metals permit the delivery of anticancer agents in a controlled and targeted manner, circumventing limitations of conventional chemotherapy. As a result, carrying drugs through nanoplatforms made of platinum has become an intense research area.

Conclusion: As nanomaterials with eco-friendly properties have been developed, they are being used in many different fields, such as biomedical engineering and drug delivery. There are many advantages to platinum NPs, such as antitumor and antibacterial activity, making them suitable candidates for a variety of pharmaceutical applications.

Keywords: platinum nanoparticles, cancer therapy, drug delivery, cancer

Adverse effect of miRNA function induced by single nucleotide polymorphism on the occurrence of uveal melanoma (Review)

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Introduction: The ocular and adnexal structures comprise approximately 5 % of all melanomas. Around 95% of ocular melanomas are uveal in origin, whereas primary conjunctival and orbital melanoma are very rare. Uveal melanoma is the most common primary intraocular malignant tumour. In the current study, we have researched the negative effect of a common single nucleotide polymorphism (SNP: rs1222227623) while converting A to G at the seed match of miR-27a-3p to 3'UTR sequence of PATZ1 gene. The PATZ1 (POZ/BTB and AT Hook Containing Zinc Finger 1) is a Protein Coding gene involved in Androgen receptor signalling and Co-regulation of Androgen receptor activity pathways.

Methods: For this purpose, GSE27831 selected from GEO dataset microarray studies was used to obtain the top differentially expressed genes though uveal melanoma. The David Database was used to cluster genes and identify the ones involved in the transcriptional regulatory pathway in cancer, including the PATZ1 gene. The relationship between studied miRNA and SNP was shown in miRNASNP-v3 database.

Results: The results showed that the miR-27a-3p blocks gene's expression, and acts as a tumour suppressor in uveal melanoma by binding to the 3'UTR region of PATZ1 gene. The occurrence of rs1222227623 (A/G on chr19:13836466) at the seed match of miR-27a-3p to PATZ1 made the binding to be lost. It makes the gene not to be under the control of miRNA anymore and upregulation will occur in gene.

Conclusion: Thus, our data suggest that rs1222227623 could be a disease-associated SNP (dSNP). It is a common polymorphism in miR-27a-3p, which affects the regulation of PATZ1 gene and results in the genetic predisposition to uveal melanoma. Its role in tumour genesis through somatic mutation preliminary evidence suggests that these effects are mediated through target genes which expressions are affected by the SNP status.

Keywords: uveal melanoma, PATZ1, miR-27a-3p, rs1222227623

An investigation of rs7903146 polymorphism in TCF7L2 gene in patients with type 2 diabetes mellitus (Research Paper)

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Introduction: The rs7903146 polymorphism in the TCF7L2 gene is the most common polymorphism associated with type 2 diabetes mellitus. The aim of this study was to investigate the association between rs7903146 polymorphism in the TCF7L2 gene and type 2 diabetes mellitus in the population of Eest Azerbaijan Province, Iran.

Methods: A number of 101 blood samples were collected from patients with diabetes mellitus and 101 from healthy individuals. PCR and electrophoresis were performed after DNA extraction and quality assay of all samples with specific primer. Finally, PCR products were treated with Rsal restriction enzyme and re-electrophoresed and the target polymorphism was investigated. Finally, PCR products were treated with Rsal restriction enzyme and re-electrophoresed and the target polymorphism was investigated.

Results: The frequency of genotypes was calculated as TT = 33.7, CC = 16.8 and CT = 49.5 (percent) for healthy individuals and TT = 43, CC = 14 and TC = 43 (percent) for patients. The percentage of T allele in healthy individuals and patients was 42.1% and 64.5%, and the percentage of C allele in healthy individuals and patients was 57.9% and 35.5%, respectively.

Conclusion: There is possibly an association between the rs7903146 polymorphism in the TCF7L2 gene and the risk of diabetes mellitus. Therefore, further studies in this field can provide more accurate results and examine the diagnosis of the possibility of developing diabetes in different populations.

Keywords: polymorphism, rs7903146, TCF7L2, type 2 diabetes.

Analytical study of the diversity of medicine use and underlying disease based on the temperament of individuals in the community (Research Paper)

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Introduction: Today, the medical world is facing a growing incidence of chronic diseases. In recent years, a person-centered medical approach to health care has emerged. Therefore, according to the individual characteristics, it is possible to take appropriate health and medical interventions for that person. Many holistic medical schools pay special attention to persons' differences with each other in the field of health, and most of their health care prescriptions are based on personal differences. According to the approach of focusing medical sciences on personalized medicine, the biological response of each person can be different from the other people and can be significant effect on the incidence and severity of the disease as well as the response to treatment. Traditional Iranian medicine categorizes many of the physical and mental differences of human societies in terms of "temperament".The balance of these mixtures harmonizes the organs of the body, which results in health. Depending on, it is possible a tendency to accept or reject a particular type of disease, or a difference in how one responds to a particular drug or stress. Thus, the influence of the individual characteristics in determining the type of response to environmental stress can be acknowledged; That is, different people may respond differently.

Methods: In this regard, a study was conducted based on the analysis of drug consumption patterns and underlying disease in people with their temperament. The object of this study was to identify the temperament patterns in the population and to determine the relationship between the use of medicine and health. This is a cross-sectional descriptive study and the statistical population of the study includes 300 healthy and sick people in Tehran. Demographic information questionnaire and temperament determination questionnaire to determine warmth, cold, wetness, and dryness of temperament were completed and the data were analyzed by chi-square test.

Results: As the findings and the level of significance of the K2 test show, there is no significant relationship between the two variables of medicine use status and different natures of individuals (P> 0.05). In addition, the degree of continuity of this relationship based on the Kramer coefficient is 0.179. This indicates that different groups without and with medicine use show relatively similar reactions to different temper. This study did not show a clear and significant relationship between healthy and unhealthy individuals and possible medicine use with their temperament.

Conclusion: Further studies with higher sample sizes in different climatic regions are suggested to further investigate the possibility of this relationship.

Keywords: Medicine- Disease- Temperament

Antibiotic resistance and human health risks. A Review (Review)

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Introduction: Antibiotics are widely used to improve human, animal, and plant health. Antibiotics, with antimicrobial activity, can cause the development of antibiotic-resistant genes and antibiotic-resistant bacteria. The main genetic mechanisms that lead to antibiotic resistance are mutations and the gaining of new genetic material. Genes encoding antibiotic resistance in bacteria can be located on various genetic components in bacterial cells such as genomic DNA (internal resistance), plasmids, transposons, and integrons. Antibiotic resistance can be achieved using four main strategies: 1) decreased membrane permeability to antibiotics, 2) antibiotic inactivation, 3) rapid release of antibiotics, and 4) change in target sites of antibiotics (such as mutations). The distribution of ARGs may be affected by many factors, including antibiotics, heavy metal ions, wastewater, several seasonally sensitive factors (rainfall, bird migration), and physical forces (such as water and wind, including erosion and rock washing). The aquatic environment is a receptive source of antibiotics and antibiotic-resistant genes and an ideal environment for bacterial growth and horizontal gene transfer. Exposure of the skin while swimming in surface water with antimicrobial agents can occur through scratched skin and wounds or mucous membranes. Studies have reported that bird droppings carry large amounts of ARGs. In addition, antibiotic-resistant genes (ARGs) can be propagated among species through horizontal gene transfer (HGT). This HGT occurs when antibiotic resistance encoded by a genetic material is placed on motile genetic agents such as plasmids, transposons, or integrons to be exchanged between microorganisms. This transfer pathway allows resistance genes to be transferred to a larger part of the bacterial community in a specific environment. ARGs can also be transmitted to their microbial offspring via vertical transfer (VGT).

Methods: This study has performed by searching the â€œPubMed databaseâ€□ and â€œGoogle scholarâ€□ by different combinations of terms â€œantibioticâ€□ and â€œresistanceâ€□. Antibiotics and their effects on environment were investigated.

Results: Antibiotics, because of their capacity to alter the structure and function of microbes, can affect the microbial community and endanger human health. This has led to public and environmental health concerns. Recent studies have shown that water (surface water, effluent, etc.) can be considered as reservoirs for the transmission and spread of antibiotic-resistant bacteria (ARB). Therefore, the release of ARB into wastewater and surface water can be dangerous to public health.

Conclusion: ARGs have attracted some attention in recent years, however, there is still a need for more effort to reduce the possibility of ARGs entering and spreading into the environment.

Keywords: Antibiotics, Antibiotic resistance, Environment.

Application of Silver Nanoparticles with Biotechnological Processes in Bacterial Resistance (Review)

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Introduction: Introduction: AgNPs are now widely used as an outstanding antimicrobial agent with great antibacterial properties. They answer a number of the requirements that new antimicrobial technologies are expected to meet to be effective, including antimicrobial performance, rapid action, and low cytotoxicity; and, finally, nanoparticles may be modified to provide selectivity and delivery to specific targets. Silver has long been utilized as an antibacterial agent, either alone or in combination with other technologies. potential to limit bacterial growth when used as silver nitrate or silver sulfadiazine in burn and ulcer creams and dressings Because of the existing understanding and evidence of silver's antibacterial activity, the research of AgNPs' antibacterial ability was an obvious path with the advent of nanotechnology. AgNPs' antibiotic potential is linked to their numerous modes of action, which attack germs in multiple structures at once and allow them to kill a variety of bacteria. The goal of this research is to see how silver nanoparticles can be used in biotechnological processes to combat bacterial resistance.

Methods: Search Method: This study is entitled Particles Application of silver nanoparticles with biotechnological processes in bacterial resistance, which were analyzed by searching scientific databases such as Science Direct, Springer, Google Scholar, PubMed

Results: Result: Currently, the literature supports three ways by which AgNPs exert their antibacterial effect, which has been seen simultaneously or independently. The first proposes that AgNPs act at the membrane level by penetrating the outer membrane and accumulating in the inner membrane, where the nanoparticles' adherence to the cell causes membrane instability and degradation, increasing membrane permeability and causing cellular content leakage and death. AgNPs have also been shown to bind with sulfur-containing proteins in bacteria's cell walls, potentially causing structural damage and cell wall rupture. The second mechanism proposes that nanoparticles can not only break and cross the cell membrane, altering its structure and permeability, but also enter the cell, where it is suggested that, due to their properties, AgNPs will have an affinity for sulfur or phosphorus groups present in intracellular content such as DNA and proteins, altering their structure and functions. They may also affect the respiratory chain in the inner membrane by reacting with thiol groups in enzymes, causing reactive oxygen species and free radicals to form, causing damage to intracellular machinery and initiating the apoptotic pathway. The release of silver ions from nanoparticles, which, due to their size and charge, can interact with cellular components, affecting metabolic pathways, membranes, and even genetic material, is thought to occur in parallel with the other two mechanisms.

Conclusion: Conclusion: The results showed the use of AgNPs reduces the amount of antibiotic and nanoparticle doses required to produce effective antibacterial action against a variety of bacteria, lowering the risk of side effects. Nanoparticles can form complexes to act as drug or antibiotic carriers, improving their release and selectivity; nanoparticles can be functionalized with different molecules to improve their antibacterial effect; and finally, they have antibacterial activity against a variety of bacteria, including Gram-negative and Gram-positive bacteria, as well as resistant strains.

Keywords: Key words: Nanoparticles, Bacterial Resistance, Biotechnological, Silver

Applications of Biosensors in Parkinson's diagnosis (Review)

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Introduction: One of the most common age-related neurodegenerative diseases after Alzheimer's disease (AD) is Parkinsonâ€™s disease (PD). The diagnosis of Parkinson's disease depends on clinical prognosis. The loss of neurons that are compressed in the substantia nigra pars compacta (SNpc), causes PD, Which is one of the main pathological features of the PD. However, laboratory tests are not yet available for definitive diagnosis of PD.

Methods: Biosensors are cost-effective, analytical devices used to detect biomarkers in a non-aggressive way. They can provide more accuracy and broader range of applicability with faster response and lower costs compared with clinical diagnosis. Biosensors usually consist of a biological sensing element that can convert the biological response made by binding target analyte and sensing biomolecule to electronic signal. Biomarkers are cellular or molecular variations that measuring them in biological media (blood, urine, etc.) can lead to diagnosis, causes and progression of a disease. There are various types of biomarkers used to study different disorders. Different types of biomarkers (clinical, pathological, imaging, biochemical) can be used in the study of PD.

Results: In this study, the use of biosensors in detecting some biomarkers which indicates PD were investigated.Â DJ-1 protein is a potential neurodegeneration biomarker. The biosensor developed to detect it is a ITO/AuNP/11-AUT/MWCNT/anti-DJ-1 neuro-biosensor, with DJ-1 antigen as the sensing unit.Â Â Â Protein DJ-1 is made by instructions that contain the genes Park7. The Park7 gene plays an important role in antioxidant defense that protects cells from oxidative stress and has been identified as Parkinson's disease. Studies show that loss of the function of DJ-1 protein is closely related to PD and can lead to this disease.Â Â Î±-synuclein is The main protein involved in PD. It is a protein that is found a lot in the brain and is abundant and more expressed in nerve tissue. The nature of this protein is Lewys amyloid in PD. Î±-synuclein Increases transmitter release from the presynaptic terminal, so it plays an essential role in synaptic plasticity and synaptic transmission. However, the physiological role of Î±-syn is unclear. Acute symptoms of pathogenesis occur in PD when improper accumulation or Î±-syn fibrillation in Lewy bodies. To monitor Î±-synuclein, a biosensor was developed based on graphene with a combination of glutamic acid and gold nanoparticles, and antibody joined with.Â

Conclusion: Diagnosis of PD is usually based on clinical examinations and motor symptoms. But the problem is when these symptoms occur, itâ€™s at the middle of the disease stage. Accordingly, itâ€™s vital to be able to diagnose PD before in early stages to help the path of the treatment and boost the

lifestyle.Â Thatâ€™s why biosensors are important. Theyâ€™re able to detect biomarkers, which are indicators of PD development before it gets severe and shows clinical symptoms. Another advantage of them is more accuracy and quicker response. Also, biosensors are easy to build and operate. They have fully defined and controllable structures at the nanoscale, They are also cheaper, and their use is significant. The sensitivity and diagnostic quality of biosensors increases due to the use of applied nanomaterials and graphite and gold nanoparticles. Some other biosensors are also developed to monitor biomarkers that analyzing them can help to control disease progression and adjust dose of the drugs. These biosensors can also become real time devices that constantly monitor biomarkers like L-Dopa and also dopamine, which play a significant role in PD progression.

Keywords: Biosensors, Parkinsonâ€™s disease, Dopamine, Neurodegenerative diseases, Biomarkers.

Aptasensors as the Promising Test Strips for Sensitive Detection of Aminoglycosides (Review)

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Introduction: Aminoglycoside antibiotics are effective clinical drugs derived from Streptomyces species or generated synthetically that include the diverse sub-classes, such as kanamycin, tobramycin, gentamicin, neomycin, and so on [1, 2]. Aminoglycosides are extensively utilized to prevent or treat bacterial infections through binding to their prokaryotic ribosomal sites that results in the mRNA mistranslation, message readout imperfection, and finally, bacterial cell death [3-6]. The marvelous inhibition effect to bacteria makes aminoglycosides advantageous in therapy, pharmaceutical industry, fishery, etc. However, their overuse arouses some serious problems for environmental safety and human health. The accumulation of aminoglycosides in human body causes the inevitable threats, such as renal toxicity, hearing loss, respiratory failure, and allergic reactions [7-9]. Hence, many organizations have determined the maximum residue limits (MRLs) of the aminoglycosides as their maximum allowable concentration (in Î¼gkg-1) in foodstuff and drinks. For example, European Union (EU) has determined the MRL range in the aminoglycoside sub-classes from 50 Î¼gkg-1 for gentamicin to 20000 Î¼gkg-1 for apramycin [10, 11]. Consequently, monitoring of aminoglycosides is very important for human safety. There are diverse conventional analytical methods for the exact detection and quantitative measurements of aminoglycosides, such as gas chromatography (GC), liquid chromatography (LC), liquid chromatography-mass spectrometry (LC-MS), solid-phase extraction (SPE), and high-performance capillary electrophoresis (HPCE). Despite their high accuracy, the methods are intricate and time-consuming under the restrictions on high cost, cumbersome sample preparation, operational complexity, and poor anti-inference that make them impractical for rapid and on-site aminoglycosides detection [12-14]. Therefore, new strategies for the simple, sensitive, selective, and rapid detection of aminoglycoside are intensively desired. To achieve the requirement, biosensors are introduced as the efficient additions to analytical sensing assays with the high potential for the quantitative high-throughput target monitoring. The enzyme-linked immunosorbent assays (ELISA) are applied as the common biochemistry test strips for the rapid target detection. Unfortunately, the deficiencies of limited lifetime, instability, difficulties in storage, susceptibility to sample matrix, and irretrievable enzyme denaturation under the harsh experimental conditions restrict their application [15-19]. Hence, aptamers have been introduced as the efficient biorecognition elements for designing aptamer-based biosensors (aptasensors). Aptamers are short synthetic oligonucleotide sequences, obtained by SELEX (systematic evolution of ligands exponential enrichment) artificial screening method. They capture the specific targets with high specificity and binding affinity through conformational

changes. Aptamers possess multifarious advantages, such as cost-effective and facile synthesis, adaptive modification, and high stability in diverse experimental conditions that convert them to the promising segments for biosensing assays [20-22]. Despite of the usage of aptasensors for the highly sensitive detection of targets, there is still an urgent requirement for facile, portable, user-friendly, and disposable point-of-care (POC) diagnostic assays. Hence, microfluidic biosensing devices have received a great attention as the equipment-free lab-on-chip approaches for the robust consumer diagnostics, particularly in the regions lacking laboratory analytical tools. The supreme characteristics of microfluidic assays such as low-reagent consumption, high-throughput, and rapidity accompanied with significant features of aptasensors provides the opportunity to design microfluidic aptasensor platforms for the highly sensitive on-site diagnostics [23-27].

Methods: Review

Results: Review

Conclusion: Aminoglycoside class of antibiotics are matters with the strong lethal features against gram-negative bacteria and some gram-positive ones. The accumulation of aminoglycosides in human body causes nephrotoxicity, ototoxicity, allergic reactions, respiratory failure, intestinal diseases, etc. Hence, developing sensitive strategies are essential for the on-site diagnosis of aminoglycosides. Specially, aptasensors have been introduced for this purpose with applying aptamers as the biorecognition segments. With providing the advantages of simple operation, low-cost, high stability, no immunogenicity, biocompatibility, and rapid detection, aptasensors are potential for portable sensing tools. Hence, a combination of aptamers with microfluidic assays, liquid crystals, nanomaterials, and smartphone technology is promising for monitoring of ultra-low levels of aminoglycosides. References 1. Edson, R.S. and C.L. Terrell. The aminoglycosides. in Mayo Clinic Proceedings. 1999. Elsevier. 2. Hermann, T., Aminoglycoside antibiotics: old drugs and new therapeutic approaches. J Cellular molecular life sciences 2007. 64(14): p. 1841-1852. 3. Vicens, Q. and E. Westhof, Molecular recognition of aminoglycoside antibiotics by ribosomal RNA and resistance enzymes: an analysis of xâ€• ray crystal structures. Biopolymers: Original Research on Biomolecules, 2003. 70(1): p. 42-57. 4. Auerbach, T., A. Bashan, and A. Yonath, Ribosomal antibiotics: structural basis for resistance, synergism and selectivity. TRENDS in Biotechnology, 2004. 22(11): p. 570-576. 5. Tor, Y., The ribosomal A-site as an inspiration for the design of RNA binders. Biochimie, 2006. 88(8): p. 1045-1051. 6. Purohit, P. and S. Stern, Interactions of a small RNA with antibiotic and RNA ligands of the 30S subunit. Nature, 1994. 370(6491): p. 659-662. 7. Zhou, Y., et al., Development of fluorescent aptasensing system for ultrasensitive analysis of kanamycin. Journal of Luminescence, 2020. 222: p. 117124. 8. Azadbakht, A. and A.R. Abbasi, Impedimetric aptasensor for kanamycin by using carbon nanotubes modified with MoSe 2 nanoflowers and gold nanoparticles as signal amplifiers. Microchimica Acta, 2019. 186(1): p. 23. 9. Xing, Y.-P., et al., Label-free detection of kanamycin based on a G-quadruplex DNA aptamer-based fluorescent intercalator displacement assay. Scientific

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Keywords: Aptasensor; Aminoglycosides; Antibiotic detection; Nanoparticles

Bacterial production and purification of human His-tagged IL-1RA and its digestion with TEV protease (Research Paper)

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Introduction: Cytokines are small cell-signaling proteins which secreted by some cells like monocytes and macrophages. IL-1 family consists of 11 members including Interleukin-1 Î± (IL 1Î±), Interleukin-1 Î² (IL 1Î²) and IL 1 receptor antagonist (IL 1RA). IL-1 is a potent pro-inflammatory cytokine that activates the immune responses against infection and inflammation by stimulating lymphocytes B and T. IL 1RA is a natural inhibitor of IL 1Î± and IL 1Î² and blocks the IL-1 receptor type I, in competition with IL-1Î± or IL-1Î². Considering, IL-1RA is unable to recruit the second receptor subunit IL-1 Receptor accessory protein (IL-1Racp), therefore the signaling pathways are not activated. The recombinant form of this protein is now available in the pharmaceutical market called Anakinra. This medicine can reduce the effects of the autoimmune diseases and also moderate inflammatory responses in patients with rheumatoid arthritis and infectious diseases. Based on the previous studies, this protein is produced mostly as insoluble form in E. coli. Accordingly, the present study was designed to construct an expression vector containing the coding sequence of human IL-1RA derived by T7 promoter into pET15b. Besides, an expression cassette of thioredoxin driven by T7 promoter was also inserted at downstream of IL-1RA cassette (TrxA). His-tag and TEV recognition site were also inserted upstream of the IL-1RA coding sequence. The recombinant IL-1RA protein in SHuffle T7 express E. coli was successfully produced into soluble form under an optimized induction condition 30Â°C, 4h and 0.5 mM IPTG. The biological function of this recombinant protein will evaluated in the future. The purpose of producing this protein in SHuffle was enhancing the capability of correctly fold proteins with multiple disulfide bonds in the cytoplasm of this strain. After purification with Ni-NTA, the purified His-tagged IL-1RA was digested with TEV protease to remove His-tag. The purpose of removing His-tag was reaching the pharmaceutical quality of IL-1RA protein in order to compare with a bioactive commercial IL-1RA protein. This study might provide a platform to produce IL-1RA protein in commercial scale in the future

Methods: In this study, the recombinant vector named pET15b/IL-1RA/TrxA was successfully constructed and transformed into SHuffle T7 strain. The soluble form of IL-1RA/His-tag was produced in SHuffle T7 strain E. coli and purified with Ni-NTA. Following-purification of His-tagged IL-1RA using imidazole, the His-tag was digested by TEV protease and removed. Imidazole is a potent inhibitor of TEV cleavage activity, so that the sample was first

dialyzed with 5% glycerol to remove 250 mM imidazole. Then it was digested with TEV protease in a reaction buffer including 50 mM Tris-HCl (pH 8.0), 0.5 mM EDTA, and 1 mM DTT at 30Â° C and for 5 h. In order to improve digested pure IL-1RA, the cleaved His-tags were removed using Ni-NTA. On the other hand, EDTA as a main component of TEV reaction buffer can chelate nickel ions in the affinity gel. Thus, the digested sample was dialyzed for the second time with 5% glycerol solution before purification with Ni-NTA. After that, the digested IL-1RA was separated in the flow-through during purification, and the success of this process was evaluated using SDS-PAGE.

Results: Based on our results, the purified IL-1RA/His-tag indicated a band corresponding to the molecular weight (Mw) of approximately 18.8 kDa. As it was shown in the lane 3, after cleavage of His-tag using TEV protease, IL-1RA protein with Mw of 17 kDa, was observed with apparent difference compared to IL-1RA/His-Tag with Mw of 18.8 kDa. After dialysis of IL-1RA to remove EDTA in TEV reaction buffer, the target protein was successfully recovered and the protein lost during dialysis steps was not significant (Lane 1, 2 and 4). The dialyzed IL-1RA was re-purified with Ni-NTA and was observed in the flow-through due to the elimination of His-tag (with Mw 17 kDa), whereas the remaining undigested IL-1RA/His-Tag was detected in the elution.

Conclusion: In this study, for the first time IL-1RA/His-Tag was produced in soluble form in Shuffle T7 strain E. coli and His-Tag was successfully eliminated via TEV protease activity. The yield of protein production was highly determined as 9.3 mg/L. The results of this study could pave the way for large scale production of IL-1RA for therapeutic applications in the future.

Keywords: Human IL-1RA, Recombinant protein, Shuffle T7 express E. coli, Ni-NTA, TEV protease.

Bacteriophages and biotechnology: Antimicrobial Therapy and Vaccine Development (Review)

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Introduction: In recent years, due to the importance of designing the most effective vaccines approach to cure illnesses, phages and phage-based vaccines are extremely vital and play the main role in medical trials. It has been recognized that bacteriophages have many different applications in the modern biotechnology industry: they have been proposed as delivery vehicles for protein and DNA vaccines; gene therapy delivery vehicles; alternatives to antibiotics; for the detection of pathogenic bacteria; and as tools for screening libraries of proteins, peptides or antibodies. In the eukaryotic hosts, phages are inert particulate antigens and cannot trigger pathogenesis so that they do not affect the human cells. Vaccines typically contain one or more adjuvants, used to boost the immune response so that the immune system can recognize the phages which were not accessible to find before

Methods: In the last decade, many studies have been explored about using phages as Nano-medicine platforms for developing vaccines due to their unique biological characteristics. The whole phage particles can be used for vaccine design in the form of phage-displayed vaccines or phage DNA vaccines. Phage DNA vaccines are the eukaryotic promoter-driven vaccine genes inserted in the phage genomes, which are carried by phages to the target cells to generate antigens. The antigens, either as the immunogenic peptides or proteins displayed on the phages or as the products expressed from the vaccine genes, can serve as vaccines to activate immune responses for disease prevention and treatment. It is hoped that scientists, clinicians, and biotechnologists currently researching or putting phages to practical use are able to expertise and thereby accelerate progress towards further development in this field of biotechnology.

Results: Both phage-displayed vaccines and phage DNA vaccines promise a brilliant future for developing vaccines. This review presents the recent advancements in the field of phage-based vaccines and their applications in both the prevention and treatment of various diseases. It also discusses the challenges and perspectives in moving this field forwards.

Conclusion: According to the importance and the applications of phage-based vaccines, However, there are problems with the stability of these vaccines, their transport, targeted delivery, safe use, and side effects. In this Review Article, experimental phage therapy based on viruses replicating in bacterial cells currently offers a chance for development in the treatment of bacterial infections.

Keywords: Bacteriophage, Phage-based Vaccines, Phage displayed vaccine, Phage DNA vaccine, Treatment

Bioinformatics evaluation of MSH2 gene in the incidence of colorectal cancer in patients with HNPCC (Research Paper)

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Introduction: Hereditary Nonpolyposis Polyposis colorectal cancer (Lynch syndrome/HNPCC) is one of the most common syndromes that predisposes colorectal cancer. The inheritance method of this syndrome is autosomal dominant. Studies have shown that lynch syndrome can be associated with colorectal cancer and tumors that originate outside the colon, including endometrial cancer. The aim of this study was to find the association between MSH2 gene and colorectal cancer through bioinformatics study

Methods: For this purpose, the miRNAs and SNPs involved with MSH2 gene were studied in the miRdSNP database. The GeneCards database was used for evaluation of drug targets. The Interactions between proteins were identified in the STRING database. The GEPIA2 database was analyzed to investigate the expression of MSH2 gene in colorectal cancer

Results: Based on the findings of GEPIA2, the MSH2 gene is highly expressed in colon cancer. The hsa-miR-21 can downregulate the expression of MSH2. The hsa-mir-137 can play a role in controlling the expression of the MSH2 gene through UTR'3, and any disturbance in this regulatory process can cause tumors in the colon. The STRING database showed that MSH6 and MLH1 have the most interaction with MSH2. All three of which are involved in the development of HNPCC syndrome. The mutations in the MSH2 gene in Lynch syndrome increase the incidence of colorectal cancer and aspirin can be a potential drug in CRC

Conclusion: Various studies have shown that mutations in four mismatch repair genes (MMR) such as (MSH2, MSH6, MLH1, PMS2) whose functions are lost during the mutation are involved in colorectal cancer in Lynch syndrome. The miRNA associated with gene can also be used for drugs that are effective in preventing colorectal cancer in HNPC. The identification of this gene is very important in identifying individuals at risk, especially those who have the Amsterdam criteria and this feature can be considered for medicinal purposes.

Keywords: miRNA-21, Lynch syndrome/HNPCC, bioinformatics prediction

Bioinformatics study of genetic pathways influenced by miR-146a in cancer incidence (Research Paper)

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Introduction: MicroRNAs are small non-coding molecules, which play regulatory roles in post-transcriptional gene expression. In this study, miR-146a genetic pathways were investigated in different types of cancer by using bioinformatics databases.

Methods: Focusing on bioinformatics aspects, miRbase and GEO databases were used to determine chromosomal profile and target genes of miR-146a. MiR-146a subcellular location and its level of expression in different organs in a healthy and tumorous state were evaluated in the GeneCards and GEPIA2 database. Finally, the DAVID database was used for genetic pathways analysis.

Results: MiR-146a gene is located on chromosome 5q33.3. This gene is expressed in different organs and cell components and it plays a regulatory role in the post-transcriptional pathway of 1442 predicted genes. Furthermore, among these gene expression pathways, by mutations in 106 cases such as APC, Ki-ras, E2F, BCL2, and WNT genes, a variety of cancers can be caused, including Endometrial cancer, Bladder cancer and Prostate Cancer. It was also identified that miR-146a plays an important role in signaling pathways such as P53, ErbB, Ras, TNF.

Conclusion: Current study reveals that miR-146a plays a regulatory role in post-transcriptional pathway of a large number of genes. It also plays an important role in some intracellular signaling pathways.

Keywords: Pathways in cancer, miR-146a, Intracellular signaling pathways

Bioinformatics study of miR-let-7c as a tumor cell biomarker for detection of bladder cancer (Research Paper)

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Introduction: MicroRNAs are small non-coding molecules, which plays a regulatory role in post-transcriptional gene expression. In this study, using bioinformatics databases, expression levels, target genes, subcellular location and genetic pathways of miR-let-7c were investigated as a bladder tumor cell biomarker for detection of bladder cancer.

Methods: Focusing on bioinformatics aspects, miRbase and GEO databases were used to determine chromosomal profile, target genes and validation of miR-let-7c as a bladder tumor cell biomarker. MiR-let-7c subcellular location and its expression levels in different organs especially the bladder in a healthy and tumorous state were evaluated in the GeneCards and GEPIA2 database. Finally, the DAVID database was used for genetic pathways analysis.

Results: MiR-let-7c gene is located on chromosome 21q21.1.The miR-let-7c is overexpressed in bladder cancer, so that it is abundantly expressed in different parts of the cell and plays a role in the post-transcriptional pathway of 2224 predicted genes of cell components. Furthermore, of the 1612 predicted miR-let-7c gene targets, which with mistakenly acting on these genescould lead to variety of diseases, it can cause bladder cancer by effecting on 85 genes. It was also identified that the most important subcellular location of miR-let-7c is in plasma membrane. According to the results, miR-let-7c can be widely found in bladder tumor cells.

Conclusion: Current study reveals that miR-let-7c plays a role in the post-transcriptional pathway of a large number of genes. It is also highly expressed in bladder tumor cells. As a result, miR-let-7c has a great potential for clinical diagnosis of bladder cancer.

Keywords: Bladder cancer, miR-let-7c, Tumor cell biomarker

Bioinformatics study of the correlation between gene expression, race and survival in patients with LUSC(lung squamous cell carcinoma) (Research Paper)

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Introduction: Studies have shown that the incidence of LUSC) lung squamous cell carcinoma(is related to various environmental factors, including race. However, the related molecular mechanisms have received less attention. In this study, the identification of genes whose expression changes are related to cancer and patients' race, as well as the relationship between the expression of these genes and survival rate.

Methods: TCGA data were used to identify the expression of altered genes in LUSC) lung squamous cell carcinoma(and the relationship between gene expression and patients' race. For this purpose, OncoDB database was used and gene expression was normalized by TMP method. To compare the groups, cancer samples were first evaluated compared to normal. The similarity between genes with different expression in cancer and genes affecting patients' races was also examined. Finally, the correlation between the desired genes and patient survival was investigated.

Results: The results of expression differences between cancer samples compared to normal showed that 1000 genes were significantly ($p > 0.01$) and expressed with lLogFCl> 2 expression criteria. On the other hand, the results of the study of the relationship between gene expression and patients 'race showed that the expression of 216 genes was related to patients' race ($p < 0.0001$). Among the genes identified in the previous stages, the results showed that there were 7 genes that had both increased expression and were related to the patients' race. Among these 7 genes, only changes in PLAAT1 expression were correlated with decreased survival rate.

Conclusion: Our results show that the PLAAT1 was overexpressed in cancer samples and was related to patients' race. On the other hand, increasing and decreasing the expression of this gene leads to a decrease in survival rate. Therefore, the results of PLAAT1 can be a good treatment candidate for LUSC)lung squamous cell carcinoma(patients of African American descent.

Keywords: LUSC, race, survival

Bioinformatics study of the effect of FHIT gene on colorectal cancer cells (Research Paper)

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Introduction: Caretaker genes, ensure genome stability as a tumor suppressor gene (TSG). Fragile Histidine Triad diadenosine Triphosphatase (FHIT), which is in the same group of caring genes, usually preserves DNA and prevents its decomposition. In this study, using Bioinformatics databases, effective signaling pathways on colorectal cancer cell apoptosis and its relevance with the FHIT gene has been investigated.

Methods: In this bioinformatic study, the GEO database was used to determine the chromosomal profile, target genes and validation of the FHIT gene as a tumor suppressor gene. Complete statistics including the position, function and Expansion of the FHIT gene in distinct organs, particularly the colon was obtained by using UniGene and GeneCards database. Subsequently, the DAVID database was used to genetic pathways evaluation.

Results: The FHIT gene is most abundant in the plasma membrane and is involved in the translation of 25 types of proteins. Protein encoded by this gene implicated in purine metabolism. This gene encompasses the fragile site FRA3B on chromosome 3p14.2, where carcinogenic damage may cause aberrant transcripts. FHIT has the function of inducing apoptosis of colorectal cancer cells apoptosis via SRC and AKT1 signaling pathways. FHIT also manages apoptosis with the aid of three main AMD1, SRC, MDM2 genes. In this way AMD1 by encoding "S-adenosylmethionine decarboxylase proenzyme" repairs stem cells, SRC through Translation "Proto-oncogene tyrosine-protein kinase Src" controls apoptosis and tumor migration and ultimately inhibits MDM2-mediated proteasomal degradation of p53/TP53.

Conclusion: Present study indicates that the FHIT gene performs a main position in signaling the apoptosis pathway of colon cancer cells, while its deficiency or inefficiency lead to carcinogenic mutations in the colon tissue. As a result, the FHIT gene has impressive potential for designing colorectal cancer modern treatments.

Keywords: Colorectal cancer, FHIT gene, Tumor suppressor gene, Apoptosis

Bioinformatics study on function of NKX3-1 gene and involved miRNAs through prostate cancer (Research Paper)

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Introduction: Prostate cancer is the second most frequent cancer in men and the fifth cause of death worldwide. The NK3 homeobox 1 (NKX3-1) is a prostate-specific tumor suppressor gene, which is located on chromosome 8p. The small non-coding RNAs (microRNAs) are involved in interaction with NKX3-1 gene. In this study, function of NKX3-1 in prostate cancer and the involved miRNAs in prostate cancer was investigated using bioinformatics databases.

Methods: The expression analysis was done on GSE26910 chosen from Gene Expression Omnibus (GEO) datasets in order to find the tumor suppressor gene in prostate cancer while prostatic and normal samples were analyzed by GEO2R package. The GEPIA2 database obtained more information about NKX3-1 expression in normal and prostatic samples. The pathways involved in prostate cancer process was studied in Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway database. The interaction between miRNAs and NKX3-1 was detected by miRTargetLink 2.0. The DIANA TOOLS - mirPath v.3 was used to find the role of miRNAs in prostate cancer.

Results: KEGG pathways revealed that, BCL-2-associated agonist of cell death (BAD) affects the process of apoptosis in prostate cancer pathway. The function of BAD is inhibited and apoptosis inhibition occurs when it is phosphorylated by protein kinase B (PKB/AKT). The inhibition of apoptosis, leads the cells to tumorigenesis. NKX3-1, a tumor suppressor gene, inhibits PKB/AKT activity indirectly and prevents the pathway toward cancer in phosphatidylinositol-3-kinase (PI3K) signaling pathway. The analyzed data showed that hsa-miR-155-5p and hsa-miR-92a-3p are correlated to NKX3-1 gene. The information obtained from miRPath v.3 showed that these miRNAs are involved in prostate cancer.

Conclusion: NKX3-1 can inhibit apoptosis indirectly by its activity in PI3K signaling pathway as a tumor suppressor. Since NKX3-1 is a tumor suppressor gene, the associated miRNAs - hsa-miR-155-5p (with strong validation) and hsa-miR-92a-3p (with weak validation)- can play roles in prostatic cancer.

Keywords: NKX3-1 gene; micro-RNA; PI3K pathway; Tumor suppressor

Biosynthesis of cobalt oxide nanoparticles using bacteria (Research Paper)

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Introduction: Nowadays, more specific methods for cancer treatment, including gene therapy and the application of nanoscience and drug-nanoparticle compounds which usually lead to a better outcome, have attracted considerable attention. Nanotechnology is used to diagnose cancer at early stages, design a drug delivery system by targeting the nano-drug combination for cancer cells, and reduce the cytotoxicity to normal cells. Cobalt oxide is one of the most potent natural antioxidants and exists in two forms: Co3O4 and CoO. Various applications of these nanoparticles in medicine, such as drug delivery systems, toxicity to cancer cells, and antibacterial properties, have been studied and analyzed. Synthesis of cobalt oxide nanoparticles can be done by various methods, including chemical, physical, physicochemical, and biosynthetic methods. So far, the synthesis of green cobalt oxide nanoparticles has been done using plant extracts, fungi, and bacteria.

Methods: In brief, luminescence Vibrio bacteria were grown in Sea Water Complete (SWC) medium at 28Â°C for 2 days. After centrifugation of cultured bacteria, 100 ml of sonicated culture was mixed with 50 ml of 25 mM aqueous cobalt nitrate hexahydrate filtrates in a 250 ml flask and incubated at 90Â°C for two hours. The successful synthesis of cobalt oxide nanoparticles (Co3O4NPs) was determined based on the color change to purple. At the next step, biosynthesized cobalt oxide nanoparticles were annealed at 500Â°C for 2 hours. X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR), Scanning electron microscopy (SEM), and energy dispersive spectroscopy (EDS) were carried out for nanoparticles characterization.

Results: The XRD results illustrated the success of biosynthesized Co3O4NPs and the diffraction peaks at 2Î¸ values of 19o and 36o. The FTIR spectra characterized the functional groups in Co3O4NPs; the peaks were observed at 3445, 2924, 1010, 605, and 561 cm-1. The 3445 and 2924 cm-1 peaks could be due to â€“OH stretching from polysaccharides and Câ€“H stretching of alkanes, respectively. The peaks at 1010 and 605 cm-1 could be assigned to (Câ€“O) of the alkoxy and CH2 groups, respectively. 561 cm-1 peak might be due to cobalt oxide NPs. The results of SEM indicated that the biologically synthesized cobalt oxide nanoparticle is spherical with a 70 nm diameter. The results of EDS analysis indicated that the main elements refer to the peaks of cobalt and oxygen to be 38 and 36%, respectively, in the biosynthesized Co3O4NPs.

Conclusion: This study investigates a biological method to synthesize cobalt oxide nanoparticles using a luminescent Vibrio bacterium. The properties of Co3O4 NPs were characterized by XRD, FTIR, SEM, and EDS. Biosynthesis of cobalt oxide nanoparticles from luminescence Vibrio is considered a novel and ecofriendly method.

Keywords: Cobalt oxide nanoparticle, Biological synthesis, Luminescent bacterium.

Biotechnologic Production of Collagen Peptides with Pharmaceutical Effects by using Enzyme Immobilization (Review)

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Introduction: Introduction One of the most challenging issues facing humanity today is widespread metabolic disease. (i.e., any of the diseases or disorders that disrupt normal metabolism). Over time, as communities become more aware, more attention will be paid to health, and the demand for beneficial substances will increase. In recent years, there has been a growing interest in looking for new bioactive compounds to treat disease, including metabolites of marine origin, like Collagen, which is the predominant connective tissue protein consisting of biologically active peptides with unique biological and technological properties. Bioactive peptides are linear or cyclic polymers composed of amino acids that are covalently bonded together. Bio-peptides are inactive in maternal protein but theyâ€™ll show their health effects after releasing, so that they can be widely used in medical, food and pharma industries. Biological properties of oral collagen hydrolysates include antioxidant activity, anti-diabetic activity , anticoagulant activity, antihypertensive activity, antidepressant activity, immune system booster and skin care. All of the above make collagen a valuable substance that can be used as an element with high therapeutic effectiveness with the emergence of problems such as increasing social age and its consequences, like chronic degenerative metabolic diseases with high morbidity and mortality rates caused by its complications.

Methods: Methods Collagen hydrolysis is performed to increase its biological effectiveness. Enzymatic proteolysis of animalâ€™s by-products using proteases (including papain, trypsin, chymotrypsin, alcalase, pepsin, and collagenase) is a rapid, reproducible and controllable method. Immobilization of enzymes conduct to expand their application and to ensure reuse in various type of process, can be defined as trapping an enzyme (biocatalyst) in a separate phase that is set apart from the main phase. Enzymes are multifunctional catalysts which immobilization can solve the issue of enzyme instability. Immobilized enzymes are trapped either physically or by covalent bonds by chemical methods in a neutral solution matrix or transporter. In other words, immobilization define as limiting the position of enzymes. If the use of enzymes in immobilization form makes the enzyme more stable, it will be possible to use an enzyme source multiple times and easily separate it from the mixture. These days, immobilization and use of various enzymes in various industries has increased. The characteristics of substrates and the conditions of enzyme immobilization have a significant effect on the enzyme activity and performance; therefore, should be selected in such a way that the goal of enzyme maintaining properties and increasing its efficiency is achieved. Mass transfer can also lead to a decrease in enzyme activity, which should be considered. Enzyme immobilization allows access to some kinetic advantages

that in some instances are necessary to get the desired product, avoiding side-reactions. Undoubtedly, future strategies will be aligned with enzyme stability in solutions, stability to contaminants, stability in the face of pH changes and tolerance of higher temperature range As most enzymes are relatively unstable and costly to isolate, the use of a method by which enzymes can be recovered or reused has become a concern for biotechnologists. Due to the outstanding catalytic properties, the properties of the enzyme must be improved before use on an industrial scale, and the enzyme immobilization method can be used to achieve the goal of improving efficiency.

Results: Result The aim of this study is to evaluate feasibility of producing bioactive peptides from collagen using enzyme immobilization method and finally trying to form this strategy on an industrial scale and focus on systematic quantification of collagen hydrolysates. Recent advances in pharmaceutical industrial biotechnology have made it possible to use immobilized enzymes for a variety of industrial and manufactural applications. These applications have a wide variety of research areas in the field of enzyme immobilization in a large number of approaches that are aligned with enzyme immobilization.

Conclusion: Conclusion Biotechnological producing of collagen hydrolysate is important in two aspects; first, confront worldwide problem of epidemic proportions by utilizing the unique physiological and biochemical properties of bio-peptides in order to prevention and treatment metabolic disorders; and, secondly, the ability of achieving same products in maximum efficiency by using less energy. According to above; Collagen has become a promising and effective tool to deal with nutritional and health deficiencies of the population. Research in the field of biotechnological processes is developing and helping to advance them as quickly as possible, and it is hoped that it will help the health of the international community.

Keywords: Enzyme Immobilization, Pharmaceutical Biotechnology, Collagen Peptides

Biotechnology and its achievements (Review)

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Introduction: Biotechnology is the product of the integration of biology with technology. Medical biotechnology is one of the newest and most effective disciplines in biotechnology. It is used to make drugs, recombinant vaccines and find ways to treat cancerThe purpose of this study is to investigate medical biotechnology and its achievements.

Methods: The present study is a review of relevant information from med Pub, Scopus, Scholer Google and Magiran Searched.Data analysis was performed qualitatively.

Results: Using medical biotechnology, protein therapy and other biological drugs can be used for Produced the treatment of many diseases. Medical biotechnology has been able to counteract other methods by producing recombinant vaccines against live and non-living viruses, ways to treat cancer using gene therapy, preventing the aging process and stem cell failure.

Conclusion: Today, ensuring the health of residentsEarth through the production of medical biotechnology With advances in biotechnology, scientists are now producing recombinant vaccines, pharmaceuticals, finding cures for incurable diseases, and diagnosing various diseases more quickly and effectively. Products produced by medical biotechnology have been able to play a significant role in this field by influencing the quality of human life.

Keywords: biotechnology, medicine, vaccine, cancer.

Biotechnology applications in thrombotic diagnosis (Review)

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Introduction: Multiple mechanisms are involved in clot formation and prevention of bleeding in the human body. In contrast, there are regulatory mechanisms including endothelial anticoagulant, antithrombin III, thrombin, and thrombomodulin to remove the clot and prevent its movement and thrombosis. However, pathological processes such as vascular disorders due to aging or cholesterol deposition, dysfunction or several coagulation factors, and platelet disorders affect the physiological balance in the homeostasis process and increase the risk of thrombosis. Diagnosis of thrombosis is very complex due to the variety of factors that upset this balance and is important because of its direct association with life-threatening diseases such as heart attack and stroke. Therefore, in this article, we want to review the diagnostic tests for thrombotic diseases and the application of biotechnological achievements for uses of in of these tests.

Methods: Search for keywords such as thrombosis, platelets, biotechnology, and the name of thrombosis diagnostic tests have been done in various databases such as PubMed, Science Direct, and Google scholar. According to criteria such as the English language and the novelty (2015_2022) of the articles, the articles are selected and then studied and their abstracts are taken in the direction of the intended purpose.

Results: In general, diagnostic laboratory tests for thrombosis are divided into two main groups; general and specific: General tests: Bleeding time (BT): The time to stop bleeding is measured and monitors platelet function. Clotting time (CT): Clotting time is the time it takes for clots to form. As a result of this test, coagulation factor dysfunction is effective. Closing time (CT): Closing time (CT) is also known as "in vitro" bleeding time. CT is evaluated using a platelet function analyzer (PFA-100Â®) and is now available as an alternative to clinical laboratory bleeding time testing. Reptilase Time (RT): This test examines plasma clotting activity based on the enzymatic function of batroxobin. Of course, there are some more general tests such as; PT, PTT, FT, and TT that

evaluate quality and quantity of coagulation factors. Specific tests: D-dimer: D-dimer is a fibrin biomarker that can be found in whole blood or plasma. D-dimer levels are elevated in diseases linked to thrombosis. Protein C & Protein S: Protein C and S are natural anticoagulants and their low level is associated with thrombosis Light Transmission Aggregometry (LTA): This method examines changes in light transmission due to platelet aggregation that occurs by adding an agonist to platelet-rich plasma. Whole-Blood Impedance Aggregometry: This method measures the change in electrical impedance between two electrodes when platelet aggregation in whole blood occurs in response to an agonist. Flow cytometry: Flow cytometry is a technique for analyzing single cells in solution quickly and with multiple parameters. Flow cytometers use lasers as light sources to generate scattered and fluorescent light signals, which are detected by photodiodes or photomultiplier tubes.

Conclusion: All general tests are performed for primary screening but CT (closing time) and RT tests are superior to other general tests. The Closing time test is done with the PFA100 device by removing maximum human error and new methods of biotechnology and genetics are used in the RT test process, but because both are not sensitive enough to detect platelet anomalies, especially thrombosis, they will push us to more specific tests with higher sensitivity. Early diagnosis of thrombosis in emergency patients at high risk of stroke is an important goal and the D-dimer test by the biotechnology of Latex agglutination and ELISA is considered the first step toward this goal. Since the test cannot show the exact location of the clot and in some cases its surface elevation under non-thrombosis conditions, it needs further tests as supplementary. Ultimately, we have tests that are most beneficial from biotechnology. The recent technology added to the LTA test that has minimized the need for personnel has increased the accuracy of the result by reducing the error percentage. However, the time-consuming test has been influenced by variables, and the need for high blood volume in it compared with EIA has made EIA preferable. Finally, the unique accuracy and minimal flow cytometry limitations that have an effective relationship with the biotechnology achievements that are applied in it make it preferable to other tests.

Keywords: thrombosis, platelets, biotechnology, thrombosis diagnostic tests

Can Curcumin Nanoparticles be Effective in Breast Cancer Treatment?: A comprehensive review study (Review)

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Introduction: Nowadays, breast cancer is known as one of the major malignancies that cause millions of deaths every year globally. Among women, this malignancy is the most prevalent cancer worldwide, with more than 2 million new cases and nearly 1 million deaths in 2018. Novel studies have been indicated that natural products can be effective anti-tumor agents. In this way, Curcumin, or diferuloylmethane, demonstrated some anti-tumor effects which inhibit cell proliferation, induce apoptosis, and act as a potent anti-angiogenic, anti-invasive, and anti-metastatic agent. On the other hand, nanoparticles as hydrophobic molecules increase the stability and bioavailability of compounds and minimize possible adverse effects. Therefore, in the current study, we have been reviewed the possible role of Curcumin Nanoparticles in Breast Cancer Treatment.

Methods: A comprehensive search was conducted in electronic databases including Embase, Pubmed, Scopus, and Web of science with the keywords â€œBreast Cancerâ€□, â€œCurcuminâ€□, â€œnanoparticlesâ€□, and all other related MeSH terms up to March 2022. Either original or review studies were reviewed to determine the Curcumin nanoparticles' effectiveness, its role, and potential toxicity in breast cancer treatment.

Results: In fact, breast cancer is divided into five major molecular subtypes including luminal A-like, luminal B-like human epidermal growth factor receptor type 2 negative (HER2â€“), HER2-enriched (non-luminal) and luminal B-like HER2+, and triple-negative. Significantly Curcumin-nanoparticles can reduce tumor weight, inhibited cancer cell proliferation, and increased tumor apoptosis and necrosis. These effects were observed in various ranges of nanoparticles such as micelles, polymeric, and lipid-based nanoparticles. Moreover, Curcumin- nanoparticles can decrease cancer stem cell population and prevent angiogenesis in tumoral tissues, which can lead to tumor death. By the way, there have been many gray areas in terms of the effect of Curcumin-nanoparticles on specific subtypes of breast cancer. Moreover, the revised studies were reported the low level of the Curcumin- nanoparticles cellular toxicity. In detail, this therapeutic agent had safe effects on hematological markers, biochemical markers, and organ damage.

Conclusion: Although many studies support the therapeutic effects of Curcumin-nanoparticles in breast cancer treatment, there are some critical gray areas in this field that need further investigation.

Keywords: Breast Cancer, Curcumin, Nanoparticles

Chimeric Antigen Receptor(CAR) T-Cell Therapy : Current and Future (Cancer, Autoimmune disease and Viral infection) (Review)

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Introduction: Chimeric antigen receptor (or CAR) T-cell therapy, is a brand new shape of immunotherapy that makes use of specially altered T cells to extra especially target cancer cells, they may become a useful and effective therapy in the treatment of autoimmune diseases like Multiple sclerosis (MS) and lupus or Viral infection such as Human Immunodeficiency Virus (HIV). The immune system is the bodyâ€™s protection against infection and cancer. it is made of unique cells and organs that defend the body from infection and most cancers. Immune cells or antibodies can be produced inside the laboratory beneath tightly controlled situations after which given to patients to treat most Cancers, Autoimmune diseases, and Viral infections. This personalized â€œLiving Drugâ€• can be effective in opposition to some human diseases.

Methods: A search became carried out in PubMed with the keywords "Chimeric Antigen Receptor" and "CART cellâ€• . The documents of interest were selected, and an essential review of the facts became completed. Chimeric Antigen Receptor (CAR) T-cell therapy entails genetic amendment of patient's autologous T-cells to express a CAR specifically for a tumor antigen, observed through ex vivo cell enlargement and re-infusion returned to the patient. CARs are fusion proteins of a particular single-chain fragment variable from a particular monoclonal antibody and one or extra T-cell receptor intracellular signaling domains. This T-cell genetic change might also occur through viral-based gene transfer techniques or nonviral strategies. which includes CRISPR/Cas9(a simple two-component system used for effective targeted gene editing), DNA transposons (â€œjumping genes", that can move and integrate to different locations within the genome), or direct transfer of in vitro transcribed-mRNA by electroporation (a powerful tool for transient genetic modification of cells).

Results: Chimeric antigen receptor T (CAR-T) cell therapy has appeared as an efficient solution for relapsed or refractory "liquid tumors" Leukemia and Lymphoma. The medical achievement of CAR T-cell therapy in blood cancers has generated enthusiasm for checking out the technic in solid tumors. but, the biology of solid tumors is more complicated than that of hematological malignancies. This type of immunotherapy has revolutionized the treatment of oncological diseases, and the potential uses in autoimmune diseases (Multiple sclerosis â€œMSâ€• and Lupus) have lately been defined. CAR-T cell is a drug that may induce HIV expression. This therapy can provide immune surveillance to â€œkillâ€• latently infected cells in response to agents.

Conclusion: In this review, the principle design of CARs, the main genetic modification techniques, the potential uses in the treatment of most Cancers,

Autoimmune diseases, and Viral infections are described. Chimeric Antigen Receptor T-cell clinical trials have generated incredible consequences inside the early results of CAR T-cell therapy sufferers with blood cancers. They may become a useful and effective therapy in the treatment of autoimmune diseases like Multiple sclerosis (MS) and Lupus or viral infection such as Human Immunodeficiency Virus (HIV).

Keywords: chimeric antigen receptor T cell CAR-T cell therapy Immune therapy living therapy cell therapy

Cloning, expression and purification and antigenicity of recombinant PilS2 protein from Pseudomonas aeruginosa (Research Paper)

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Introduction: Introduction Pseudomonas aeruginosa is an opportunistic and gram-negative bacterium that is one of the most important causes of nosocomial infections. Although many advances have been made in the treatment of Pseudomonas aeruginosa infections, infections caused by this bacterium are still one of the leading causes of death in human societies. Various pathogens such as lipopolysaccharide, pili, alginate, flagellum, and proteases are involved in the pathogenicity of this bacterium. Type IV pili as an important virulence factor in this bacterium are divided into three subtypes that according to the available reports, subtype b of the fourth type pili (PilS2) can be a significant target in therapeutic and preventive studies and of infection by this bacteria should be considered. The aim of the present study was to design, induction, and purification of this protein in a recombinant form. The production of this recombinant protein could be the prelude to the design of an effective vaccine based on a specific antibody against the PilS2 binding region, which may be used as a practical strategy to prevent Pseudomonas infection.

Methods: Methods Escherichia coli (E.coli) has been used as an efficient system for expressing recombinant PilS2. The constructed recombinant pET-28a-pilS2 vector into the E.coli BL21 expression system and protein was expressed as inclusion bodies following induction with IPTG. Solubilization of inclusion bodies in urea was followed by refolding of protein in nickel affinity chromatography. The refolded histidine-tagged PilS2 protein was purified and eluted from the column using imidazole and its purity was confirmed by SDS-PAGE. Western blotting was used to investigate the antigenicity of the recombinant protein.

Results: Results PilS2 recombinant protein was highly expressed after induction by 100 mM IPTG at 37 Â°C for 3.5 h in E. coli BL21 host cells. Observation of a 17 kDa protein band on SDS-PAGE gel was an indication of protein expression. Western blotting showed that the recombinant protein was properly produced and purified and formed a single band on the nitrocellulose membrane after exposure to the antibody.

Conclusion: Conclusion Based on the results of this study, the recombinant PilS2 protein was produced properly. This protein can be used in future studies to study immunogenicity against Pseudomonas infections.

Keywords: Keywords PilS2, Pseudomonas aeruginosa, Type IV pili.

Common drugs used from December 2019 to March 2022 for COVID-19 disease (Review)

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Introduction: In December 2019, a group of pneumonia caused by an emerging coronavirus (2019-nCoV) appeared in Wuhan, Hubei Province, China. Initially, it was called the coronavirus, but due to differences with other families in the group, it was renamed the emerging corona, but today it is called COVID-19. The first case of the disease was reported in Wuhan, China, which was initially linked to an unauthorized market for the sale of animal feed but was later denied. The genomes of various animals were then examined, and some anteaters and bats were suspected, but the CDC (Center for Disease Control and Prevention) has not yet officially stated what the primary source of the virus was. Coronaviruses(CoV)belong to the coronaviridae family and are classified as nidovirals. Coronavirus is divided into four genes: alpha, beta, gamma and epsilon. Alpha and beta coronaviruses are found only in infected mammals, while gamma and epsilon are the primary source of infected birds with a small number of infected mammals. Human coronaviruses include alpha coronaviruses (229E and NL63), beta coronaviruses (OC43 and HKU1), Middle East Respiratory Syndrome Coronaviruses (MERS-CoV), Acute Respiratory Syndrome Coronaviruses (SARS-CoV) and2019-nCoV. 2019-nCoV belongs to the genus Beta coronaviruses. Current studies have shown that 2019-nCoV is derived from wild animals, but its exact origin has not yet been determined. It will be possible with accurate sequencing of the virus gene after the end of the current pandemic. General treatment strategies include rest and supportive care. Getting enough calories and water, keeping your body hydrated and homeostasis, monitoring vital signs, oxygen saturation; Respiratory and oxygen inhalation are required; Blood and urea levels, C-reactive protein and other biochemical indicators of blood, including liver, kidney, myocardial enzyme function are critical to the patient's condition. The use of antiviral and anti-inflammatory drugs for other diseases is essential.

Methods: The PubMed, Google Scholar, and Scopus databases were searched to find studies, and 14 articles were studied.

Results: Because there was no drug or vaccine to treat COVID-19 at the beginning of the disease pandemic, various clinical trials on some anti-viral drugs for other diseases and treatment of rheumatoid arthritis were important in improving hospitalized cases of 2019-nCoV in hospitals and preventing further deaths from the disease. Research has shown that drugs can inhibit clarinet-induced endocytosis, thereby inhibiting viral infection of cells. Baricitinib acts as a high-affinity NAK inhibitor for AAK1, centrally regulating clarinet-mediated endocytosis. This drug could be useful against SARS-CoV-2 infections due to appropriate clinical trials. Baricitinib, Fedratinib, Ruxolitinib are potent and selective JAK inhibitors approved for infections such as rheumatoid

arthritis and myelofibrosis that were used at the onset of the disease. Interferon-alpha is used as a broad-spectrum anti-viral drug to treat HBV, and its effectiveness has been investigated. Lopinavir / Ritonavir was used to treat adult patients with 2019-nCoV. Chloroquine and Hydroxychloroquine have been approved by the US Food and Drug Administration (FDA) to treat malaria, lupus, and rheumatoid arthritis. Still, initial research in human and primate cells has shown that these drugs can effectively treat COVID-19. Various anti-viral, anti-inflammatory and immunosuppressive drugs, anti-parasitic (ivermectin), etc., were used in patients admitted with COVID-19 in the early years of the disease.

Conclusion: At the beginning of the epidemic, there was no specific drug or vaccine for 2019-nCoV. All drugs were based on SARS, MERS, previous flu treatments, rheumatoid arthritis and HIV treatments, and immunosuppressive drugs. Numerous clinical trials have been performed on high-efficacy drugs until an approved drug with higher efficacy was found to treat COVID-19. Baricitinib is the effective combination of the anti-HIV lopinavir with ritonavir, Remdesivir, hydroxychloroquine with azithromycin, and immunosuppressive drugs, the effectiveness of which has been briefly confirmed in research.

Keywords: COVID-19, Pandemic, Treatment

Comparing efficiency of cell free DNA and exosomal DNA as non-invasive screening method in prenatal diagnosis (Review)

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Introduction: Prenatal genetic diagnosis relies on invasive methods to obtain fetal material suitable for analysis, such as amniocentesis and chorionic villi sampling. These procedures carry a small but significant risk of fetal loss, as well as risk to the mother alone (around 1% â€“ 2% of cases). The discovery of cell free fetal DNA (cffDNA) and exosomal DNA (exoDNA) in the blood of pregnant women leads to immediate recognition as an alternative source of fetal material for prenatal diagnosis. It also leads to the formation of a novel field of non-invasive prenatal diagnosis (NIPD).

Methods: In this article, we aim to summarize the fast-growing evidence for cffDNA and exosomal DNA as minimally invasive screening method in prenatal diagnosis and to highlight their opposing diagnostic advantages and disadvantages.

Results: Placenta trophoblast cells are known to release cell-free DNA (cfDNA) into maternal circulation, which are DNA fragments of 160-170 base pair. The concentration of placental cfDNA in plasma, also known as the fetal fraction, is on average 10% of the total plasma cfDNA, and increases with gestational weeks. Trophoblast cells also release exosomes into maternal circulation. Exosomes are a type of extracellular vesicles (EV) that contain constituents (protein, DNA, and RNA) of the cells that secrete them. In 2018, the existence of exosomal DNA (exoDNA) in the exosomes of maternal blood was proven. They could identify fetal exoDNA in the exosomes extracted from maternal plasma. ExoDNA show shorter fragments yet lower fetal fraction than cfDNA. The median fragment size of exoDNA is 152.4bp with the standard deviation of Â±10.51bp and the exosome concentration positively correlates with gestation weeks. cell-free DNA (cfDNA) became a sensitive biomarker for detection of fetal DNA (cffDNA) in noninvasive prenatal test. ExoDNA shared some similar features to plasma cffDNA and could potentially be used to noninvasively detect fetal conditions such as chromosome aneuploidy and single gene disease. It has been proven that, exoDNA could be used to determine fetal gender correctly, and all trisomies as well as mutations that cause genetic diseases in fetus. CfDNA is known to be a fragmented DNA and prone to nuclease activity in the circulation. The estimated half-life of cfDNA in the peripheral blood ranges between 4 min and 12 h. this short half life forcing fast protocols of sample collection. On the contrary, EVs and their cargo show a considerable long-term stability in body fluids that facilitate their analysis in biobanked samples. Maternal plasma contain not only maternal but also fetal exoDNA. Although the fetal fraction of exoDNA have a nice correlation to that of cfDNA, it is significantly lower than cfDNA and with weak relationship to gestational weeks. Theoretically, using the placenta specific markers such as PLAP, pure placenta-derived exosomes can be specifically isolate. This may raise huge

benefits to develop novel NIPT methods to detect copy number variation and monogenetic disease in fetus, since the high fetal fraction of placental exoDNA can overcome the current NIPT limitations that are mainly caused by the mixture of maternal-fetal cfDNA and low fetal fraction. CfDNA has proven remarkable performance in next-generation sequencing techniques (NSG) and studies based in gene-wide analysis (GWA). Nowadays, the use of PCR-based assays that can simultaneously assess multiple regions of driver genes and droplet digital PCR enables screening tests of fetal deasease.

Conclusion: Although, both exoDNA and cfDNA could be applied to the noninvasive prenatal studies with a real-time PCR method and other DNA quentity assessing methods and the use of EV-DNA did not lead to improved sensitivity or better detection of prenatal disease, considering the known difficulties during isolation and stability of cfDNA, exosomes might provide a new opportunity for prenatal diagnosis and screening.

Keywords: cell free fetal DNA (cffDNA) exosomal DNA (exoDNA) non-invasive prenatal diagnosis (NIPD)

Comparison of the effect of aloe vera gel and 1% silver sulfadiazine cream on the healing of second degree burn wounds (Research Paper)

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Introduction: Aloe vera has traditionally been used to heal burns, but clinical evidence remains unclear. Today, due to less side effects and cheaper medicinal plants, their consumption is increasing. This study was performed to compare the effect of aloe vera gel dressing and 1% silver sulfadiazine cream on the healing of second degree burn wounds.

Methods: This clinical trial was performed in Peimanieh Hospital in Jahrom. 50 patients with second degree burn wounds were selected and randomly divided into experimental and control groups. 25 patients were treated with aloe vera gel and another 25 patients were treated with 1% sulfadiazine silver cream daily. Using the Bets Jensen Wound Assessment Tool, the parameters related to burn wounds on the first, seventh and fifteenth days were examined. Use SPSS software version 17 and repeated measures analysis of variance statistical software to check the obtained information.

Results: In the experimental group, the mean improvement status at the beginning of the study decreased to 30.515 with a standard deviation of 0.316 and on the fifteenth day to 13.303 with a standard deviation of 0.516 and in the control group at the beginning of the study 31.219 with a standard deviation of 0.321 and on the fifteenth day to 19.188 with a standard deviation of 0.524. On the 15th day, a significant difference was observed between the two groups

Conclusion: Aloe vera gel can be a good alternative due to the complication of 1% sulfasiazine silver cream in partial inhibition of epithelialization and discoloration in the wound area.

Keywords: effect ØŒ aloe vera gel ØŒ 1% silver sulfadiazine cream ØŒ healing ØŒ wound

Computational Biology of COVID-19, Comparative analysis of codon usage, and phylogenetic relations (Research Paper)

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Introduction: Coronaviruses are enveloped single-stranded RNA genome viruses causing respiratory distress syndromes. Open reading fram1a (ORF1a) encodes the enzymes of the RNA-synthesizing for replication of viral genome and synthesis of subgenomic mRNA. The aim of the present in-silico study was to compare codon usage, rare codon clusters and phylogenetic relations in COVID-19 coronaviruses.

Methods: The nucleotide sequences and their features of the Coronaviridae family were obtained from NCBI and frequency, number and fraction of 61 codons for each amino acid was evaluated in the structure of viral protein and the preferred codons were assessed using Gene Infinity website. The variation in codon usage bias were quantified by the ENC and CBI in the ACUA software.

Results: Finally, evolutionary relationship and phylogenetic analysis of Coronaviridae were studied using the MEGA 7 software. The GC3% of the cds was in the range from 15.668 to 16.534 and GC3 Skewness from 0.299 to 0.34. Analysis of codon usage for all of amino acid in COVID-19 showed considerable differences between the viruses. The findings of the present study revealed that the patterns of base compositions in COVID-19 are most likely the result of mutation pressure rather than that of natural selection, since at all codon positions its effects are present.

Conclusion: In addition, analysis of base composition it was found that the cds of COVID-19 are rich in AT, which should be considered in designing new drugs.

Keywords: Computational Biology, Coronaviruses, codon, Coronaviridae

correlation between BP1 and SPL1 and protein phosphorylation in spms(multiple sclerosis) (Review)

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Introduction: MS, as a chronic autoimmune disease with unknown etiology, is the most common neurological disorder in young adults. It is characterized by the infiltration of auto-reactive immune cells into the central nervous system (CNS), which leads to inflammation, demyelination, and axonal degeneration. Several studies suggest that genetic, environmental, epigenetic and infectious factors may contribute to the etiology and pathogenesis of MS. This essay survey death ratio reason of SPMS patient.

Methods: In order to start this study, we used GEO accession number GSE131282. In our work, we focus on patient with less disease duration , then by the use of GEO2R web tool, we analyzed the information. Eventually, for every gene list we removed differentially expressed genes (DEGs) which had p-value more than 0.05 and log 2 FC between Â±0.6. protein-protein interaction (PPI) was used to find the proteins that is coded by DEGs, thereby string data base was utilized for this aim. The list of DEGs was deposited in this data base and output, PPI network, was received. To analyze PPI networks, Cytoscape 3.4.0 and Gephi software v 0.9.1 were used to visualization of networks.

Results: samples of patients and controls were compared to identify DEGs in each disease. The number of DEGs were 801 genes in SPMS which 356 were upregulated and 484 were downregulated. Analysis of modules and their functional annotation in SPMS show G-protein coupled receptor signaling pathway and extracellular matrix organization and etc.

Conclusion: this essay demonstrated that BP1 and SPL1 play crucial role in mortality of SPMS. positive regulation of gene expression and protein phosphorylation have limited in case of PPMS.

Keywords: #multiple_sclerosis#SPL1 #BP1

CRISPR Cas Technique: A New Way of Genetic Disorder Treatment (Review)

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Introduction: Modification of defective and non-functional genes is called gene therapy. This therapeutic phenomenon was first proposed in 1990 by Rosenbey et al. There are various genes therapy techniques such as Crispr and Lenticular Viral Transmission System. In the Crispr technique, Mendelian genetic diseases were at the forefront of treatment. The latest findings of gene therapy researchers were treatment in patients with beta-thalassemia major and tuberculosis anemia. However, this method has been used to treat cancer binaries, diabetes, and the production of recombinant vaccines. It has also been used in the rapid diagnosis of Covid-19 patients. Diabetes treatment With Crispr cas 9 methods, multipotent germ cells called CyT59 can be used to transform and transform pancreatic islet cells; Consequently, it was used to treat type 1 diabetes (T1D). This action takes us one step towards achieving an effective treatment for type 1 diabetes to target immune cells that destroy insulin-producing cells in the pancreas; Treat this type of autoimmune disorder. Production of new antibiotics with the help of Crispr With the help of Crisper, a mutation can be made in bacteria and actinomycetes without the need to break double-stranded DNA. This failure causes weakness and instability in the bacterial genome, forcing it to rearrange the gene and, in some cases, remove much of its chromosome; In this way, new bioactive and antibiotics can be produced against them. Preventing the progression of throat cancer with the help of Crispr Researchers at the University of Griffith in Australia used CrisprK9 to treat neck cancer with the papillomavirus, or HPV, in mice. Human papillomavirus (HPV) infections are the leading cause of most throat cancers. The virus inserts two specific genes, E1 and E1, into the human genome that can cause cancer, which is the best target for Crisper. Crisper tracks a specific DNA section containing cancer genes, cuts it, and then removes it and replaces it with a benign, harmless agent. In this example, scientists instead of adding more information distorts the gene; Nanoparticles find cancer in cancer cells and expose it to some DNA The excess that causes misreading and then stops the protein from being made. This is similar to adding an extra word to a word that the editor does not recognize. In this experiment, the crisper set was placed inside the nanoparticles, and then the mixture was injected into infected mice. The results were amazing; The tumors in the treated mice completely disappeared, and the animals survived. Mice also showed no signals or side effects such as inflammation. This method's possible side effects include altering genes that have not been studied, and occurring Signs of silent mutations noted. It is hoped that with the advancement of technology in this field, Crisper can be used to treat a variety of cancers. Crispr: A way to fight RNA viruses Many incurable diseases have viral causes, including Ebola, Zika, and the flu. A team of researchers at MIT and Harvard University has tested the CRISPR RNA-Cutinary enzyme method on an antiviral agent that can be programmed to detect and destroy RNA viruses in human cells. Researchers

have previously used the Cas11 enzyme as a tool for cutting and editing RNA and as a detection method to track the presence of viruses, bacteria and other targets. This study is one of the first uses of KAS11 on cultured human cells. Researchers have combined Cas11 antiviral activity to detect and track it and use a new system that can be used to diagnose and treat viral infections, including infections with a newly discovered viral agent. They call it (CARVER; The 11-or-11-Casin-Assisted Restriction of Viral Expression Readout is called viral expression and readout. Human pathogenic viruses are very diverse and adapt to their environment continuously and without the need for any viruses, which emphasizes both the challenge and the need for flexible antiviral drugs. CARVER has been established as a fast programmable detection method and anti-virus technology for a wide variety of viruses. The need for a new antivirus is essential. Over the last 50 years, 95 clinical antiviral drugs have been developed that can cure only 9 diseases, and this is also important; Pathogenic viruses evolve rapidly and change their genome and adapt to their environment, resulting in their resistance to the drugs produced. Case 11 enzyme naturally targets viral RNA within bacteria; For this reason, this enzyme can be used as an antiviral therapy to target specific sequences and sequences of low-restriction RNA and its relatively easy access into, including human cells. In this study, scientists after screening RNAs Viral, looking for duplicate sequences that were least likely to mutate during cutting; In order to disable the virus, they did. Case 11 can program for almost any part of the virus, but due to the wide variety of viral species and the occurrence of rapid genomic changes called viral evolution, there is a possibility of error in selecting the incision site, which can be ineffective at best. So far, thousands of sites in the hundreds of thousands of viruses that have been targeted by 11 people; has been identified. In this study, the activity of ces11 in human cells infected with one of the distinct RNA viruses was investigated; Lymphocytic Chriomeningitis Virus (LCMV), which is a positive single-stranded adenovirus, influenza A or IAV virus, and blister virus and VSV first expresses the Case-11 gene and, with the help of a synthetic and engineered RNA guide, enters the culture medium and after 95 hours is exposed to viruses and after 95. Another hour Cas11 enzymes reduced viral RNA levels in cultured cells twisted more than 55 times.

Methods: By searching in various databases.

Results: e Cas9 system can be used in a wide range of genomic manipulations. Genetic manipulation generally refers to all the processes that target and modify genes within a cell. Genetic manipulation is the basis of many scientific, biotechnological, food and human activities. Establishment of more than 42 major companies in the United States, Europe and Asia since 2015, focusing on treating human genetic diseases using Crisper-Case 9 technology, promising new horizons in treating deadly genetic diseases such as muscular dystrophy or viral infections such as HIV and hepatitis.

Conclusion: With Crispr's advanced and precise technique, a dramatic revolution in treating diseases has taken place. In this method, we hope that common multifactorial diseases will also be treated in addition to monogenic diseases.

Keywords: CRISPR; TREATMENT: MENDELIAN DISORDERS

Cyanobacteria biotechnology and its applications in human health (Review)

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Introduction: Cyanobacteria are gram-negative bacteria that have been considered in recent decades due to their strong potential in the production of various therapeutical compounds and nutritious foods. Cyanobacteria have the potent capacity to adapt to the different environmental conditions as they grow and live in a variety of habitats, including extreme habitats. Additionally, their diverse conservation, biosynthetic mechanisms, and ability to symbiosis with a wide range of living creatures further make cyanobacteria capable of living in different environmental conditions. Because of their potential applications such as high biomass production, simple and cheap growth requirements and high growth rate compared to other photosynthetic organismsØŒ valuable knowledge about cyanobacteria genome and ease of genetic manipulating as well as production of a wide range of their secondary metabolites they are one of the cost-effective goals for biotechnology.

Methods: In this review article, we describe some of the bioactive properties of cyanobacteria after a literature review from reputable and up-to-date servers such as PubMed, Science Direct and Google Scholar. We also summarize the therapeutic potentials of cyanobacteria as a good natural source in biotechnological processes, citing examples of these properties.

Results: Since growing humanâ€™s need to the production of novel medicine, such as new antibiotics, antivirals and food supplements is felt, natural reservoirs can be considered as a good source of bioactive metabolites for therapeutic goals. In recent years, due to the increase of antibiotic-resistant bacterial strains, attention has been focused on new effective antibacterial compounds. Among these, the secondary metabolites produced by cyanobacteria with antimicrobial properties against Gram+ and Gram- bacteria can be mentioned. Polyketides, antimicrobial peptides (AMPs), Alkaloids, terpenes, lipids and polyphenols are most important agents with antibacterial activity. Most polyketide antibiotics have been isolated from Nostoc species. Nostocyclyne A, cylindrofridin A, the carbamidocyclophanes are the members of polyketides family with antibiotics properties. Cyanobactins are small cyclic peptides with antibacterial activity. Kawaguchipeptins A and B are known

examples of AMPs that isolated from Microcystis aeruginosa. Almost all antibacterial alkaloids isolated from cyanobacteria are indole containing compounds such as hapalindoles, hapalonamides, ambiguines and fischerindoles. Also, antibacterial terpenes from cyanobacteria have been reported. The first one is Diterpenoid noscomin that isolated in 1999 from Nostoc commune and exhibited activity against Bacillus cereus, Staphylococcus epidermidis, and Escherichia coli. Studies also showed that Fischerella strain has the potential to produce a lipid bioactive named É£â€• linolenic acid with antibacterial properties. Polyphenols isolated from Fischerella ambigua or ambigols A, B, and C displaied potent activity against several Gram+ bacteria strains. Today The emergence of viral epidemics and the lack of sufficiently effective antiviruses is one of the human concerns. Specific species of cyanobacteria produce the antiviral compounds. For example, nostoflan has been detected in the Nostoc flagelliforme, which showed potent effects on influenza A virus, human cytomegalovirus and herpes simplex virus type-1. Cyanobacteria also produce a wide range of antifungal compounds such as scytophycin (an antifungal macrolide) that has been identified in Anabaena sp. Many produced antiprotozoal Compounds or anti-parasite from cyanobacteria show significant effects against protozoans for example it has been reported tow compounds named Calothrixins A and B detected in Calothrix species that show antiplasmodial activity. On the other hand, cyanobacteria produce bioactive compounds with anticancer activities as an example, cyanobacteria Symploca sp. produces a compound called Symplocamide that shows activity against H-460 lung cancer cell line. Finally, it is important to mention that several cyanobacteria genera, such as Spirulina were also found to be rich source of nutrients, as proteins, essential fatty acids, vitamins and minerals that can be used in food supplements. Also, some secondary metabolites and pigments produced by cyanobacteria have cosmetic properties and can be used in the production of UV protection, moisturizing, whitening and anti-aging agents.

Conclusion: Cyanobacteria identified as a natural source of variable bioactive compounds such as secondary metabolites, peptides and proteins that have a various therapeutic property, including antibacterial, antiviral, antifungal, anticancer, antiprotozoal and anti-inflammatory. Cyanobacteria also can be used as a rich source of nutrients and cosmetics. Therefore, cyanobacteria can be used as an excellent source for medical and pharmaceutical biotechnology.

Keywords: Bioactive compounds, Secondary Metabolite, Cyanobacteria, Antimicrobials

Design of a Cell-Free DNA Isolation method from maternal plasma based on Metal Organic Frameworks; with the aim of use in prenatal sex determination (Research Paper)

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Introduction: Many sex-linked genetic diseases are identified in humans, with male fetuses more exposed to the complications of the diseases. So, prenatal sexing seems important in identifying these infants. Common methods are unable to define fetal gender safely, early and accurately. The use of cell-free fetal DNA has been in the focus of researchers. One of the challenges of using this method is the isolation of fetal DNA from maternal plasma. Commercial kits are expensive and offering low yield of DNA. In this project, we intend to isolate fetal DNA from maternal plasma using metal organic frameworks nanoparticles labeled with specific probes of the SRY gene specific for the Y chromosome.

Methods: Y-Chromosome Specific probes were immobilized on BIOMIL-4 metal organic frameworks (M.O.Fs) and the resulting construct was characterised using XRD and FTIR methods. These functionalized M.O.Fs were added to maternal plasma aliquots for the target DNA fragments to hybridize to the probes. Conventional and Real-Time Polymerase Chain Reaction were performed to confirm isolation of target DNA fragments.

Results: The XRD curve confirmed that immobilization of dna probes on MOFs did not alter the crystaline structure of the frameworks. The FTIR analysis also confirmed the presence of chemical bonds reflecting the presence of nucleic acids in the surface of MOFs. The PCR reaction successfully amplified targeted DNA fragments, confirming the isolation of Y chromosome specific DNA.

Conclusion: Using metal organic frameworks for immobilization of hybridization probes may be a method of interest for isolation of specific DNA fragments from clinical samples.

Keywords: Cell-free fetal DNA, Metal-Organic Frameworks, Hybridization Probes, Sex determination

Designing a multiepitope construct as a therapeutic vaccine for HPV using E1, E5, and E6 proteins (Research Paper)

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Introduction: Introduction: Cervical cancer is the fourth most frequent cancer in women worldwide. Human papillomavirus (HPV) is the most important etiological factor for this cancer. Prophylactic vaccines have no therapeutic effect against infection; therefore, it is important to use new approaches such as therapeutic vaccines. E5 and E6 oncoproteins cause proliferation. However, E5 downregulates the expression of HLA-class 1 then disrupts CD8+ cytotoxic T lymphocytes responses. Thereby, causing immune evasion. E6 suppress P53 and is responsible for transforming infected cell. E1 is essential for initiating DNA replication and is a helicase protein. It is the preferable strategy to induce a broad CTL response directed against several CTL epitopes for treatment. Using reverse vaccinology and bioinformatic tools we can predict potential T cell binding epitopes. This study aims to design a therapeutic multi-epitope vaccine construct using E1, E5, and E6 Tcells epitopes.

Methods: The reference sequence of E1 (P03114), E5 (P06927), and E6 (P03126) proteins were obtained from UniPort. To predict CTL and HTL epitopes we used netCTL 1.2 and netMHCII servers respectively. netCTL predict 9mer epitopes for 12 MHC class I supertypes (A1, A2, A3, A24, A26, B7, B8, B27, B39, B44, B58, and B62). For epitope identification in this server, 0.75 was used as the threshold. Using netMHCII we predicted 15mer HTL epitopes for HLA-DR, HLA-DQ, HLA-DP alleles. Predicted epitopes were submitted to the VaxiJen v2.0 server for evaluation of antigenicity, AllerTOP v. 2.0 server for allergenicity assessment, and ToxinPred to select non-toxic epitopes. Additionally, HTL epitopes were used for their inducibility of interferon-Î³ (IFN-Î³), and interleukin-4 (IL-4) using IFNepitope and IL4pred respectively. After selecting the final epitopes for each protein, the vaccine construct has been constructed. Ultimately, the final construct was evaluated for antigenicity (using ANTIGENpro), allergenicity (using AllerTOP v. 2.0), toxicity (using ToxinPred), and physicochemical properties (using ProtParam).

Results: Primarily, we selected epitopes that cover more MHC alleles in each protein. At least each epitope in two alleles must have the ability of MHC binding. In the next step, selected epitopes were assessed for antigenicity using VaxiJen. Epitopes with a threshold > 0.4 were considered Probable antigens. Moreover, non-allergen and non-toxic epitopes were selected for further analysis. HTL epitopes with the ability to induce IFN-Î³ and IL-4 were selected as potential epitopes. Acceptable epitopes with mentioned filters from each

protein were used in the final construct. EAAAK, AAY, and GPGPG linkers were used for linking selected epitopes. CTL epitopes were linked using AAY and HTL epitopes were linked using GPGPG linkers. Moreover, 50S ribosomal protein L7/L12 (Locus RL7_MYCTU) as an Adjuvant was linked to the construct in N-terminal using the EAAAK linker.

Conclusion: In this study, we designed a multiepitope construct with the potential to be considered a therapeutic vaccine for HPV. Epitopes were selected from E1, E5, and E6 proteins. Using proper linkers and adjuvant, we constructed a multiepitope construct that has proper physicochemical properties, it is antigenic and has no allergenicity. However, further analysis is needed to confirm the functionality of this structure.

Keywords: HPV - Human papillomavirus - multiepitope - vaccine-bioinformatic

Designing and Constructing a Novel Hybrid Photobioreactor (HPBR) For Carbon Dioxide (CO2) Mitigation via Chlorella Vulgaris Microalgae (Research Paper)

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Introduction: The Rio de Janeiro Climate Change Agenda Agreement, signed in 1992, addresses global warming and has since emphasized the importance of developing technologies to reduce or absorb greenhouse gases emissions, so much so that the final document expressed concern about rising greenhouse gas levels and the need to prevent them 20 years later. Several studies have recently assessed the ability of specific algae species to reduce CO2 emissions from industrial plants. These microalgae must be able to withstand not only high levels of CO2 but also sulfur dioxide, nitrogen oxides, and volatile organic compounds (VOCs) in waste gases.

Methods: CO2 removal was investigated in this study after designing and building the novel hybrid photobioreactor (HPBR). The amount of CO2 removal is measured and analyzed in terms of time during each period of microalgae culture. The pH, OD, dry weight (DW), and fluid retention time in the photobioreactor were determined after examining the CO2 removal process. The effect of a long retention time on CO2 removal was observed in a photobioreactor. This study had been divided into three stages; stage1: Algae culture in Erlenmeyer, CO2 removal investigation, and determination of appropriate optical cycle parameters. Stage2: Design and manufacturing of HPBR. Stage3: Investigations in the HPBR system, which all divided into two categories: (A) The effect of reactor design type on CO2 removal rate (in this experiment, three design models were considered; Bubble Colum, Air Lift, and the Novel HPBR) and (B) The effect of microalgae concentration on removal efficiency.

Results: During 14 days of cultivation within the systems, the photosynthetic performance of Chlorella Vulgaris species was investigated. The Novel HPBR achieved the highest CO2 bio-fixation rate and biomass productivities compared to the control group (Bubble Colum) and Airlift Photobioreactors. The rate of CO2 bio-fixation was 280 mg L-1 d-1, and the biomass productivity was 0.15 g L-1 d-1. The separability of this "Novel HPBR" enabled efficient cleaning and maintenance intending to increase industrialization potential. Furthermore, an additional feature of this novel HPBR enabled its application on wastewater treatment bioprocesses by taking biomass productivity into account.

Conclusion: Microalgae research for greenhouse gas removal and wastewater treatment has resulted in newly designed close systems such as photobioreactors. These are significantly efficient on both bench-scale and

industrialized applications. Considering design indices and microalgae mechanical fluid stimulated the development of the novel HMBR, which provided a higher rate of greenhouse gas removal (specifically CO2), a single construction with multiple applications, and a significantly higher rate of nitrate and phosphate removal from manciple wastewater. Furthermore, higher biomass productivity resulted in greater sustainability.

Keywords: CO2 Capture, Microalgae, Greenhouse Gas, Sustainability, Wastewater Treatment

Detection of the presence of Merkel cell Polyomavirus DNA in the serum of HBV and HCV patients compared to healthy control groups (Research Paper)

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Introduction: Merkel cell polyomavirus is a small, non-enveloped, and double-stranded DNA virus, which belongs to the Polyomaviridae family. Merkel cell polyomavirus (MCPyV) has been found in 80% of Merkel cell carcinoma (MCC), a rare but invasive form of skin cancer. Recent evidence revealed the presence of MCPyV in the serum and plasma samples of viral hepatitis patients and even healthy blood donors. There is no information about the molecular epidemiology of MCPyV in HBV and HCV patients in the world and also there is little known about the virus in healthy controls in Iran. The aim of this study was to determine the presence of the MCPyV genome in HBV and HCV patientsâ€™ blood samples compared to healthy controls, in order to evaluate the co-infection between MCPyV and hepatitis B and hepatitis C viruses.

Methods: A total of 900 serum samples, including 300 HBV, 300 HCV positive samples, and 300 serum samples from healthy controls were examined. Nested- PCR method was used to investigate the presence or absence of Merkel cell polyomavirus DNA among these samples.

Results: After reviewing HBV, HCV, and healthy control samples for Merkel cell polyomavirus DNA. Among 900 serum samples, 2 out of 300 serum samples (0.6%) from HBV patients, 1 out of 300 serum samples (0/3%) from HCV patients, and 3 of 300 healthy controls (1%) were MCPyV positive.

Conclusion: Given that MCPyV is a rare and newly known virus, we examined the presence of the MCPyV genome in HBV and HCV patients. Previous

serological evidence suggests that the virus can be found even in healthy controls. However, according to the results, the circulation of MCPyV in the serum samples is rare. Therefore, more studies are needed, especially in different groups, in order to find more information about the co-infection of MCPyV with other viruses in Iran and the world.

Keywords: Merkel cell polyomavirus; Merkel cell carcinoma; HBV; HCV; healthy control

Diagnostic methods for leptospirosis (an important zoonotic disease in Iran) (Review)

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Introduction: Leptospirosis is a common disease between humans and domestic and wild animals and is important in terms of economic impact on rural areas. Humans become infected by scratching the skin and mucous membranes following contact with contaminated water and soil in the urine of infected animals. It is associated with acute kidney damage, liver disorders, brain involvement, and pulmonary hemorrhage in humans. Leptospirosis needs warm, humid conditions to survive. The peak of the disease occurs during the warmer months of the year in temperate climates in the rainy season in the tropics.

Methods: The PubMed, Google Scholar and Scopus databases were searched for the purpose of finding studies and nine articles were studied.

Results: Diagnosis of leptospirosis is based on both clinical examinations and serological tests, including microscopic agglutination tests (MAT) and diagnosis of DNA by polymerase chain reaction (PCR) and isolation of the organism through culture methods or detection of antibodies to the organism. MAT is the most common serological test for diagnosis. This is a reference test in which all other tests are evaluated and is a diagnostic test designated for international trade. Although the MAT test is a reference method, it has limitations, including low sensitivity in the acute phase of the disease, which surface IgM rise and There is no ability to differentiate IgM from IgG.

Conclusion: Nowadays, recombinant antigen methods and molecular tests are used as alternative methods.

Keywords: Leptospirosis, MAT, PCR

Early Diagnosis of Alzheimerâ€™s Disease Using Electrochemical-based Nanobiosensors for miRNA Detection (Review)

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Introduction: Alzheimer's disease is an incurable neurodegenerative disorder and characterized by progressive memory loss and cognitive function deficits. In Alzheimer's, abnormal proteins accumulate inside and outside of the neurons, which disrupt the connection between neurons and eventually destroy certain neural cells. MicroRNAs (miRNAs) are a group of single-stranded non-coding RNAs with an average length of 22 nucleotides and are highly conserved. They effect on genes by binding to 3â€² untranslated region (3â€²UTR) of the target messenger RNA (mRNA) and regulate post-transcriptional gene expression. Because Alzheimer's is an untreatable disease, early diagnosis using reliable biomarkers is a promising way to control the disease in its early stages. In the onset of neurodegenerative diseases, imbalance of microRNA expression has been proven, which this dysregulation plays an important role in the pathogenesis of these diseases. In recent years, the use of electrochemical nanobiosensors to measure circulating microRNAs as a potential biomarkers in neurological diseases has been increasingly developed due to their low cost, ease of production and use, fast response, good stability, and high sensitivity. Accordingly, they have become attractive tools in the early detection of many diseases, including neurological diseases.

Methods: An electrochemical biosensor is usually made of a solid electrode with a single-stranded nucleotide probe or a complementary microRNA sequence on its surface and electroactive hybridization markers. Multiple carbon nanotubes (MWCNTs), gold nanoparticles (AuNPs), and graphene oxide (GO) are commonly used to increase surface area and electrical conductivity. In case of Alzheimer's, a thiol probe with the miR-137 complementary sequence, a reliable biomarker for Alzheimer's detection, can be used. For this purpose, the complementary nucleotide sequence of miR-137 should be exposed to an electrode coated with nanoparticles.

Results: The use of nanomaterials in biosensors improves stabilization, detection methods, and the sensitivity of biosensors. Due to the high affinity of the thiol groups (-RSH) to nanoparticles, especially AuNPs, functionalized AuNPs with specific oligonucleotide sequence are more stable and have a stronger binding affinity to their complementary nucleic acid sequences. After the modified nanobiosensor is exposed to a clinical sample, hybridization would occur in the presence of the target microRNA (in this case, miR-137). Under these conditions, the hybridization process is converted into a measurable signal using electrochemical techniques.

Conclusion: To date, there is no cure for neurodegenerative diseases and no gold standard diagnostic method has been defined for them. MicroRNA-based

biosensors have become promising devices due to their many useful properties, including high stability, good sensitivity, and easy production process at low cost for detecting these diseases in the early stages, especially Alzheimer's. Previous studies to make a nanobiosensors for microRNA detection in Alzheimer's have demonstrated the effectiveness of these biosensors in measuring real clinical samples and have made them as a potential tool for early diagnosis of this disease.

Keywords: Alzheimerâ€™s disease, Neurodegenerative disease, MicroRNAs, Nanobiosensor, Electrochemistry

Effect of phosphatidylserine on cirrhosis-induced hepatic encephalopathy: Response to acute endotoxemia in cirrhotic rats (Research Paper)

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Introduction: In cirrhosis, the levels of proinflammatory cytokines are high in the liver and blood. Endotoxin decreases level of consciousness in cirrhotic rats. Phosphatidylserine exists in the cell membrane structure and is essential for the survival of neurons. Phosphatidylserine receptor is found in phagocytic cells and also activates the signaling of membrane proteins in apoptotic process. Therefore this study was aimed to explore the hypothesis that hepatic encephalopathy is prevented by phosphatidylserine treatment and if so, whether this is associated with altered level of proinflammatory cytokines in the brain.

Methods: Cirrhosis was induced by surgical ligation of the bile duct in male Wister rats. The groups were treated with phosphatidylserine and saline for 4 weeks. Brain IL6, TNFÎ± and the expression of phosphatidylserine receptor were assessed. Intraperitoneal injections of either saline or lipopolysaccharide (0.1 mg/kg) were administered to each group. Finally, animal behavior, blood ammonia and the expression of toll like receptor 4 were examined in the brain.

Results: Cirrhosis in rats was associated with altered expression of toll-like receptor4 in brain cortex and phosphatidylserine treatment increases toll-like receptor4 receptor expression. Phosphatidylserine had anti-inflammatory effect in healthy rats but no effect in cirrhotic rats. Chronic phosphatidylserine treatment decreased blood ammonia in BDL cirrhotic rats treated with lipopolysaccharide.

Conclusion: The brain of cirrhotic rat is more susceptible to acute endotoxemia and chronic phosphatidylserine treatment decreases blood ammonia and encephalopathy in cirrhotic rats by encountering endotoxin. Phosphatidylserine may boost immune system against endotoxin.

Keywords: Biliary cirrhosis, Hepatic encephalopathy, Acute endotoxemia, Phosphatidylserine

Effect of various preparations of gingiva Extra cellular matrix on the surface attachment of Streptococcus mutans (Research Paper)

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Introduction: Investigating the biological phenomena in an In Vitro condition necessitates providing a test condition as close to the physiological state as possible. The surface properties of the cultivation chamber have a significant impact on the successful attachment and the subsequent proliferation of cells. Previous studies have proved that the extracellular matrix (ECM) proteins remarkably affect cellular adhesion and colonization. The potential of bacteria in adhesion and biofilm formation in the oral cavity is expected to be affected too by the ECM composition of the target tissue. The greater similarity to the target tissue, the more real results in the in vitro investigations on the oral cavity biofilms. Consequently, coating the cell culture plates and flasks with the related proteinaceous preparations seems reasonable.

Methods: In the present study, Streptococcus mutans ATCC 35668 was used as the most studied model organism in oral cavity-related investigations on biofilm formation, and its adhesion potential was compared in cell culture plates coated with various concentrations of pepsin digested ECM of gingivae, pronase E-digested ECM of gingivae, and the collagen A protein. The adhesion degree was determined by performing the MTT assay as a colorimetric method with specificity in quantifying the viable cells.

Results: Results showed that the number of viable adhered bacteria was higher when the pronase E-digested ECM was used as the surface coat in comparison to the other coatings.

Conclusion: It seems that all proteinaceous components of ECM together had a better performance in supporting the S. mutans compared to the collagen A alone. Also, the degree of enzymatic digestion and the profile of the resulting peptides might cause a difference in the adhesion efficiency.

Keywords: bacterial adhesion, culture surface coating, Streptococcus mutans, collagen A, extracellular matrix

effective factor to change spermatogenesis in multiple sclerosis (Review)

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Introduction: behavioral and cognitive disabilities are rooted in Neurodegenerative diseases are rooted in the central nervous system (CNS). abnormalities in the genome and/or metabolism in brains stems Neurodegenerative diseases such as Multiple sclerosis (MS) is a chronic disability disease which is one of common disease in the world.in this study we investigate the cause of death ratio in PPMS patient.

Methods: In order to start this study, we used GEO accession number GSE131282. In our work, we considered patients with disease duration 54 PPMS years in PPMS as control groups and disease duration 4 years as treatment groups and by the use the limma package in R software data was analyzed. differentially expressed genes (DEGs) list by utilizing string database was analyzed to build Protein-protein interaction (PPI) network. Cytoscape 3.4.0 have been software that construct modules and Gephi software visualized our network.

Results: In case of PPMS, the number of DEGs were 845 genes which 707 were upregulated and 138 were downregulated. analysis of modules shows that translation and regulation of apoptotic process are two major function. in addition, top ten of nodes determine as hubs genes such as RPL11and PLEC.

Conclusion: Our study illustrated that changing in expression of TP53 and MAPK14 and so on can affected violence of PPMS disease. Thus patient with type of intensive PPMS has drastically decrease in spermatogenesis and cell differentiation.

Keywords: #multiple_sclerosis#MAPK14 #TP53

Engineering NK Cells with RNA Interference: potential method for cancer treatment (Research Paper)

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Introduction: RNA interference (RNAi) strategies include double-stranded RNA (dsRNA), small interfering RNA (siRNA), short hairpin RNA (shRNA), and microRNA (miRNA). RNAi is a potent gene-silencing process that holds great promise in the field of cancer therapy. The discovery of RNAi has generated enthusiasm within the scientific community, not only because it has been used to rapidly identify key molecules involved in numerous disease processes including cancer, but also because RNAi has the potential to be translated into a technology with major therapeutic applications. RNAi is a simple and rapid method of silencing gene expression in a range of organisms. The silencing of a gene is a consequence of degradation of RNA into short RNAs that activate ribonucleases to target homologous mRNA. Natural killer (NK) cells are innate immune cells endowed with potent cytolytic activity against tumors, and meanwhile act as regulatory cells for the immune system. INHBA encodes an individual from the TGF-Î² superfamily of proteins and the ligand could be further homo-dimerized to shape activin A or hetero-dimerized to frame inhibin with inhibin beta B . Activin-A impaired human and mouse NK cell proliferation and reduced the production of granzyme B to impair tumor killing. Similar to TGF-ï• ¢, activin-A also induced SMAD2/3 phosphorylation and stimulated NK cells to increase their cell surface expression of several markers of ILC1 cells. So with targeting INHBA by RNAi and prevent the formation of Activin-A, NK cells can do they roles in cancer treatment.

Methods: Methods: At the First, INHBA sequence collected from NCBI, for design siRNA and shRNA used SSD software. Potential miRNAs which targeting INHBA Were identified by using Targetscan and miRDB databases.

Results: according to results we identified 7 miRs(hsa-miR-205-5p , hsa-miR-135b-5p, hsa-miR-135a-5p, hsa-miR-22-5p, hsa-miR-509-3p, hsa-miR-20a-5p, hsa-miR-20b-5p) that were Accepted in both of Targetscan and miRDB databases. siRNAs and shRNAs which designed by SSD has shown in table 1and 2). Single-targeting therapies for covid19have been considered to be an effective approach, and RNAi strategy is a better method for gene suppression, and there are many siRNA drugs in clinical trials which two or more genes inhibition simultaneously. At the same time, structurally modified siRNAs . had been widely used in the RNAi therapeutics development, especially long

double-stranded RNAs (dsRNA) were designed for carrying two or more siRNA sequences That targeted more than two parts of one mRNA or more than one mRNA. Current studies have shown that once long dsRNAs get into mammalian cells, they can be used as Dicerâ€™s substrates for siRNAs processing, then the corresponding genes may be possibly inhibited effectively by siRNAs.

Conclusion: This study has described that has RNAi the potential for cancer treatment. The field of RNAi is still rapidly growing and new discoveries are being made on a daily basis. SiRNAs are currently being used in gene function analysis, target identification and validation and as therapeutic agents. Their potential for use in evaluating target toxicity is significant and warrants further investigation. Although a viable technique for in vitro experimentation, success can still be hampered by challenges with intracellular siRNA delivery and effective gene silencing. Extra researches for choosing the best candidate for siRNA is needed. Choosing the best candidate is one of the critical steps.

Keywords: RNAi , Natural killer cells , Cancer

Estimation of tumor size by diffusion equation (Research Paper)

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Introduction: Tumors in the early stages of formation are without arteries (they do not have their own source of blood supply) and depend on diffusion from the surrounding arteries to receive oxygen and nutrients, as well as to excrete waste products. As the tumor grows, the demand for nutrients increases until the flux of nutrients through the tumor surface is insufficient for all cells in the tumor area. Therefore, tumor growth continues only when the tumor is permeable to a network of capillaries.

Methods: By considering the slope of nutrients around the tumor and the size of the tumor, we can determine the extent of angiogenesis as a result of the size of the tumor at a later time. In this article, the diffusion method is used to estimate the volume of the tumor at different times and matlab software is used to implement it in the personal system.

Results: The system determines the rate of angiogenesis and ultimately the size of the tumor based on the amount of material accumulation. By doing this, we can determine the rate of tumor growth and its risk to the patient (especially in brain tumor samples).

Conclusion: Accordingly, estimating the size of the tumor at the desired time by the system has accelerated our work for surgery and drug delivery and treatment of people with cancer. The use of this system will also give us the coordinates of how the tumor will orient and grow in a predictable way at the time we want, which makes the treatment of such diseases easier.

Keywords: Tumor, mathematical model, diffusion equation, MATLAB software, angiogenesis, surgery

Evaluate the immune properties of marine-based Collagen dressing in wound care management (Research Paper)

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Introduction: In recent years wound care products attracted much researchâ€™s attention, intending to replicate or add to the extracellular matrix (ECM), provide more patients assent, reduce healing time and costs. Wound healing consists of sequence processes: hemostasis, inflammation, proliferation, and remodeling. In delayed wound healing, the healing process stopped at one of these phases, especially at inflammation due to the prolonged existence of a high level of metalloproteinase (MMPs), which destructed healthy ECM and prevented re-epithelialization. The ECM is the major component of the dermis, which provides proteins, enzymes, growth factors, and the dynamic structure for cells that are essential for wound healing. Collagen is the abundant fibrous protein in mammalian bodies, and that is the main component in the extracellular matrix (ECM). Collagen plays an important role, in all wound healing processes, by attracting fibroblasts formation, increasing keratinocyte cells migration, and collagen deposition in the wound bed. There are many different sources for collagen extraction. But among these, fish waste is a low-cost and safe source for collagen extraction. Fishery processing provides 50% to 70% fishery waste with protein bases, which causes several environmental problems. In this article, we aimed to investigate the immune properties of marine-based collagen as a bioactive component for wound care management products.

Methods: In order to investigate the immune properties, the marine-based collagen was purchased from the Rozhan Vista Mehr Ltd group, and immune properties were evaluated by studying the in-vitro cytotoxicity test MTT, the test for in-vivo irritation, and skin sensitization. All of the examinations were conducted by Nikopharmed Arya Co laboratory.

Results: The in-vitro cytotoxicity response in L929 mouse fibroblast NCTC for the marine-based collagen showed 95.51% viability, and No reactivity in morphological grade for 24 hours. The results provide evidence to support that the Collagen, Type I is Non-Toxic. The irritation response category in a rabbit of the marine-based collagen for 72Â±2 hours was 0, so the mean score is Negligible. The results provide evidence to support that the Collagen, Type I is Non-Irritating. The sensitization response category in Guinea pigs of the marine-based collagen for 48Â±2 hours was 0, so the mean score is No visible change. The results provide evidence to support that the Collagen, Type I is Non-Sensitizing.

Conclusion: As a result, marine-based collagen demonstrated unique properties such as non-toxicity, non-irritating, and non-sensitizing, consequently the best choice as a bioactive component for wound care management and biomedical applications.

Keywords: Collagen, wound healing, fish waste, biomedical, immune properties

Evaluation and comparison of the production of the quadrivalent HPV recombinant vaccine by VLP method in two models of enveloped and non-enveloped (Research Paper)

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Introduction: By 2022, about 220 human papillomavirus (HPV) genotypes have been identified. This large group of double-stranded DNA viruses is grouped into five genera (alpha, beta, gamma, mu and nu) based on the nucleotide sequence of the major structural protein L1, and can be classified into mucosal or cutaneous types based on their preferential infection site. Generally, HPV encodes at least six early genes (E1, E2, E4, E5, E6 and E7) and two late genes (structural L1 major and L2 minor capsid proteins). E1 and E2 are important for viral genome replication and its regulation, E4 promotes virion release from keratinocytes, while oncogenes E6 and E7 interfere with the hostâ€™s cell cycle regulators to ensure viral genome replication.

Methods: To develop HPV-16 L1 / L2 chimeric protein VLPs, a neutralizing cross-epitope of the HPV-16 L2 gene was first inserted into the HPV-16 L1 gene. Chimeric L1 / L2 HPV-16 was then inserted into the pPICZA plasmid and expressed in Pichia pastoris (P. pastoris). Final purification of VLPs was performed using an ultra centrifuge (130,000 g) using a sucrose density gradient of 10-40% for 4 hours at 4 Â° C. SDS-PAGE and Western blotting were performed separately for L1-HPV-16 and L2-HPV-16 proteins. 55 ng of purified VLPs for detection of L1 HPV-16 and L2-HPV-16 antibodies by ELISA test separately coated with ELISA wells using commercial L1-HPV-16 and L2-HPV-16 antibodies Ø´Ø¯. Sera of 16 patients positive for HPV-16 and 85 serum negative for HPV infection were tested for HPV-16 antibody by ELISA and the results were compared with a commercial test kit.

Results: It can be stated with certainty that Licensed human papillomavirus (HPV) vaccines contain virus-like particles (VLPs) self-assembled from L1 major-capsid proteins that are remarkably effective prophylactic immunogens. However, the induced type-restricted immune response limits coverage to the included vaccine types, and expensive multiplex formulations, restrictive storage and distribution conditions drive the need for next generation HPV vaccines. Vaccine candidates based upon the minor structural protein L2 are particularly promising because conserved N-terminal epitopes induce broadly cross-type neutralizing and protective antibodies.

Conclusion: In vivo, there are specific mechanisms that show how antibodies produced from L1 protein and L2 protein can neutralize HPV infection. Protein

L1-raised antibody-mediated protection differs based upon antibody levels. High doses of protein L1 antibodies prevent viral BM binding leading to the Fc-mediated opsonization of antibody-bound viral particles by phagocytes, mainly neutrophils.

Keywords: human papillomavirus, HPV, VLP, protein L1

Evaluation of cancer biotechnology performance to determine new breast cancer biomarkers (Review)

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Introduction: Breast cancer is the leading cause of cancer in the world and the fifth leading cause of cancer. Deaths worldwide In 2020, breast cancer due to the accumulation of genetic and epigenetic mutations was reported as one of the most common. Types of cancers are among women. The diagnosis is made by a mammogram after a test, then tissue or fluid (biopsy) is removed from the suspected area and examined under a microscope. Early detection of cancer cells spread in the blood Environmental can help a lot in the timely treatment of the disease. While the heterogeneity of breast cancer has been observed at the molecular level, cancer cells that have spread to the peripheral blood can serve as a new marker. Clinical studies have shown an association between overexpression of the HER-2 biomarker and breast cancer. The HER-2 oncogene encodes the tyrosine kinase receptor, which plays an important biomarker role in invasive breast cancer as well as a target for the treatment of the disease. Previous studies have shown increased expression of this biomarker in tumor cells. This study aimed to evaluate the performance of cancer biotechnology to determine new biomarkers of breast cancer.

Methods: This review study was conducted in 2022 by searching for valid keywords such as Breast Neoplasm, Biological Marker, HER-2, Immunolabeling Technics, Biotechnologies invalid databases including PubMed, Elsevier, and Web of Science. Finally, 15 articles were found and 10 of them were included in our study

Results: Cancer remains a major cause of death and a major barrier to increasing life expectancy worldwide. Worldwide, there are approximately 19.3 million new cases of cancer and approximately 10.0 million deaths from cancer by 2020 [1]. The burden of cancer and mortality is rapidly increasing, attributed to aging and population growth, along with changes in the prevalence and distribution of major cancer risk factors. Women's breast cancer is currently the most commonly diagnosed cancer, with an estimated 2.3 million new cases by 2020 (11.7%), followed by lung (11.4%), colon (10.0%), prostate (7.3%) And stomach (5.6%) are cancers and the fifth leading cause of cancer death. Identification of breast cancer biomarkers in the blood using nanomaterials Physical, chemical, optical, and electronic properties of various nanomaterials facilitated the identification of these biomarkers and performance Improve diagnosis. Diagnosis of biomarkers in the blood is relatively non-invasive and can provide useful biological information that complements imaging and immunohistochemistry.

Conclusion: At present, the diagnosis is mainly done in a clinical laboratory. Transforming the current diagnosis into point-of-care testing methods will be of great benefit to the community, and assisting with cancer screening will lead to the discovery of more specific cancer biomarkers, as well as significantly contribute to the early detection of cancer.

Keywords: Breast Neoplasm, Biological Marker, HER-2, Immunolabeling Technics, Biotechnologies

Evaluation of Clinical and Therapeutic Implications of Stem Cells in the Accurate Diagnosis and Treatment of Advanced non-Cellular Lung Cancer (Review)

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Introduction: Understanding the biology of cancer stem cells (progenitor cells, CSCs) is one of the biggest challenges in basic science and clinical oncology. Lung cancer remains one of the leading causes of cancer-related deaths worldwide among men (23% of all cancer-related deaths) and women (22% of all cancer-related deaths). This common type of cancer has a variety of pathological features that are still considered a serious oncological problem worldwide. Therefore, the genetic basis of this cancer has received a lot of attention. Cancer stem cells (CSCs) are involved in the onset and progression of tumors. Spontaneous mutations accumulate in stem cells throughout a person's life, leading to the formation of CSCs. In the study, we studied non-small cell lung cancers (NSCLCs). Over the past decade, in-depth analyzes of the lung cancer genome and signaling pathways have defined NSCLCs as a group of distinct diseases with genetic and cellular heterogeneity. As a result, a substantial list of potential treatment goals was presented that drastically altered the clinical evaluation and treatment of patients. Many targeted therapies have been developed with convincing clinical evidence of the concept. However, therapeutic responses are usually short-lived.

Methods: This is a secondary study, with a narrative approach in 2022 by searching for keywords such as Mesenchymal Stem Cells, Lung Neoplasms, Neoplastic Stem Cells, Epidermal Growth Factor, and Therapeutic Equivalency in Mesh and valid databases. Others, such as PubMed, Science Direct, Scopus, and the Web of Science, conducted a search of 15 articles, of which 10 were included.

Results: According to the studies obtained from the articles, the results show that lung cancer has the highest number of cancer deaths worldwide. More than 85% of these cases are currently classified as non-small cell lung cancer (NSCLC) with a projected 5-year survival rate of 15.9%. Although histological features and expression remain the basis of clinical diagnosis of tumors, recent advances in NGS and other high-performance genomic profile platforms have allowed researchers to extensively study genetic mutations in lung tumors. Following the detection of KRAS and BRAF8, 9 mutations, epidermal growth factor receptor (EGFR) receptor mutations were detected in patients with pulmonary ADC and were associated with a response to EGFR10-13 inhibitors. The study of somatic mutations in natural tissues and their role in tumor

progression and aging offers new insights into cancer treatment. Direct studies of mutation loads, mutation signatures, clonal dynamics, and cellular phenotypes provide a bridge from epidemiological discoveries to mechanical insights into the early stages of cancer. The fluid biopsy may improve the eligibility of lung cancer patients for targeted therapies or immunotherapy by identifying appropriate tumor targets and biomarkers and better defining predictors of response to modern therapies.

Conclusion: According to the results, further studies on the tumor microenvironment have discovered new possible ways to control this deadly disease, including immunotherapy.

Keywords: Mesenchymal Stem Cells, Lung Neoplasms, Neoplastic Stem Cells, Epidermal Growth Factor, Therapeutic

Evaluation of growth and differentiation of mouse osteoblast progenitor cells on synthesized nano-hydroxyapatite bone scaffolds (Research Paper)

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Introduction: There are promising tools today for bone tissue regeneration. However, it is difficult to trace cells and maintain them at the site of injury. A potential solution is to culture the cells on bone scaffolds and then examine the source of osteoblast cells and the molecular factors that differentiate them. We used RT-PCR test to design the scaffold and then study the proliferation and differentiation of these cells. Scaffolds should have features such as controlled degradation, biocompatibility, increased cell viability, differentiation, production of extracellular matrix, food and excretory production, adhesion and integration with natural bone tissue, three-dimensional structure with internal pores associated with Both the chemical level and the surface are suitable. Tissue engineering is a growing field and can be a permanent solution for tissue damage and analysis. In this approach, cells, scaffolds and messaging factors are used. Scaffolds are three-dimensional structures that provide the necessary conditions for cell proliferation and differentiation, and their structure determines the final shape of the tissue. The aim of this project was to investigate the effect of bone scaffolds on the growth and differentiation of mouse osteoblast progenitor cells into adult osteoblasts. Hydroxyapatite with the compound Ca10 (PO4) 6OH2 due to its biocompatibility and bioactivity, is widely used in bone and tooth treatment applications and as a hard tissue.

Methods: After synthesis of bone hydroxyapatite and sodium alginate scaffolds and its characterization (tests: degradation, swelling, mechanical, porosity, (FTIR-ATR), in order to evaluate their quality, osteoblast cells were cultured on the scaffolds and In order to study the morphology of the cells on the scaffold, SEM test, MTT cell viability and expression of Runx2ALP, COL1 genes, Real-timePCR test were performed.

Results: Bone scaffold with new formulation affects mouse osteoblast cell line. And increases the expression of genes involved in cell growth and differentiation. Bone scaffolds synthesized for safe and successful use in clinical settings, biomaterials for bone tissue engineering show several characteristics such as biocompatibility, biodegradability, bone formation and bone conduction, scaffold pore structure, grain size and surface topography. Real-timePCR differentiation factors were examined to evaluate the differentiation and growth of osteoblast cells, and this issue was confirmed by increasing the expression of these genes in the study of gene expression.

Conclusion: Real-Time PCR results show increased expression of type 1 collagen genes and alkaline phosphatase and Runx2 compared to control cells. By examining the expression of genes influencing cell growth and differentiation, it can be concluded that synthetic scaffolds have the ability to optimize the substrate for the growth of mouse osteoblast cells.

Keywords: Cell scaffolding, alkaline phosphatase, osteoblasts, cell differentiation, collagen 1

Evaluation of insulin expression and toxicity of hybrid nano-liposomal extract in diabetic RINm-5F cell line (Research Paper)

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Introduction: Type 2 diabetes is a common metabolic disorder. Each year, 170 million people worldwide develop diabetes, 95% of which is related to type 2 diabetes. In this study, the effect of combined nanoliposomal plant extract (green tea, chicory and garlic) with metformin (a common type 2 antidiabetic drug) on insulin expression was compared.

Methods: Thin layer watering method was used to prepare nanoliposome structures. RINm-5F cells, which are beta cells of mouse pancreas, were obtained from the Iranian Genetic Resources Center and propagated in RPMI 1640 medium. The cells were then diabeticized with streptozotocin (STZ) and the diabetic cells were divided into 5 groups. Three groups were treated with different concentrations of combined nanoliposomal plant extracts (0.4, 1 and 2 mg / ml) for 48 hours, one positive control group receiving the anti-diabetic drug metformin at a concentration of 5 mg / ml for 72 hours. And a negative control group that were treated only with FBS. MTT test was used to evaluate the toxicity of plant extracts and then the level of insulin expression in different groups was compared by immunohistochemical test.

Results: The morphology of the cells changed after treatment with metformin or extract, especially at higher doses of the extract, and changed from epithelioid and cubic to spindle and elongated forms, which indicates more proliferation and adhesion of cells to the bottom of the culture flask. MTT test showed that the combined nanoliposomal plant extract had no toxicity to the cells and did not reduce the cell viability percentage compared to the control group. Also, the results of immunohistochemical test showed that plant extract at a concentration of 2 mg / ml significantly increased insulin expression compared to metformin (P <"0.01").

Conclusion: The results of toxicity test and insulin production showed that the combined nanoliposomal extract of the plant green tea, chicory and garlic is useful for the treatment of type 2 diabetes because, despite being less toxic, it is more effective at a concentration of 2 mg / ml compared to metformin. .

Keywords: Diabetes, nanoliposomes, plant extracts, metformin

Evaluation of the bacteria with transovarial transmission in Anopheles stephensi (mysorensis strain) for determining new candidates for paratransgenesis (Research Paper)

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Introduction: Malaria is one of the most important parasitic diseases throughout the world. The Anopheles stephensi is the main vector of malaria in Iran. WHO suggested different strategies for combatting against malaria. paratransgenesis is one of the effective solutions for developing the Global Malaria Eradication Programme. In paratransgenesis, symbiont microorganisms are manipulating genetically for blocking the parasite life-cycle, affecting the fitness and longevity of vectors. In this study, by sterilizing eggs of Anopheles stephensi and removing surface bacteria, vertically transmitted bacteria were identified in Anopheles stephensi mysorensis strain using the culture-dependent method.

Methods: An. stephensi eggs were collected from the insectary in Pasteur Institute of Iran where they were raised. Sterilization was performed by the Brundage method for obtaining the sterile seven generation. The suspension was prepared from the sterile eggs and it was inoculated into the enrichment mediums. Then, dissimilar morphological colonies were selected for performing the differential biochemical tests. Next, PCR was performed by 16s rRNA gene specific primers on isolated clones and finally sequenced.

Results: The results of this study demonstrated that the eggs of microbiota of An. stephensi mosquito were gram negative and gram positive bacteria which include: Serrratia marcescens and Asaia .

Conclusion: According to the fact that the paratransgenic technique is an effective method for eradication malaria so, introducing the suitable candidates is essential for developing this technique. Therefore, in this study, the best bacteria candidates in An. stephensi mosquito eggs that have specific features like simple transformation capacity, and transovarial transmission were identified and provided the fundamental data for developing paratransgenic technique.

Keywords: Paratransgenesis, Malaria, Anopheles stephensi.

Evaluation of the Effect of the Ni-Thiosemicarbazones complex on Expression Changes of CPEB2 gene in Acute lymphoblastic leukemia (Research Paper)

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Introduction: The aberrant proliferation and differentiation of a clonal population of lymphoid cells are involved in the pathogenesis of ALL. ALL has a poor prognosis, with only 10% of adult ALL patients surviving and 30% of pediatric ALL patients surviving. The complete remission rate in adult ALL is 30 percent to 40 percent in the first relapse and 20 to 25 percent in the second relapse with conventional chemotherapy. CPEB2 is increased in cancer tissues and increases the proliferation and migration of cancer cells of this kind. Thiosemicarbazones (TSCs) are a type of Schiff base made by combining thiosemicarbazone with an appropriate aldehyde or ketone. Chemists and biologists have been studying TSCs because of their diverse pharmacological properties. The application of these outstanding metal chelators against cancer is one of the promising areas in which they are being developed. The goal of this study was to see how Ni-thiosemicarbazone complexes affected the expression of the CPEB2 gene in a cell line that had been diagnosed with acute lymphoblastic leukemia.

Methods: In the current research, two concentrations of Ni-Thiosemicarbazone complexes were prepared: 100.5ÂµM and 104ÂµM at 24hours. The Jurkat E6.1 cell line was purchased from Pasteur Institute and treated with prepared doses of the Thiosemicarbazones complexes Ni at 24 and 48 hours after cell passage. The expression changes of CPEB2 and GAPDH were studied using Real-Time PCR after RNA extraction and cDNA synthesis. Finally, Rest 2002 Software was used to analyze the data, and Excel was used to draw the diagrams.

Results: The results of our findings showed that the expression of CPEB2 in comparison with the GAPDH housekeeping gene decreased after 24 hours of Ni-Thiosemicarbazone complexes treatment at concentration of 104 ÂµM. According to the findings, changes in CPEB2 gene expression increased after 24 hours at a concentration of 100.5ÂµM and 104ÂµM decrease were statistically significant These changes included 100.5ÂµM (0.019) and 104ÂµM (0.984) at 24 hours, respectively. (P <0.001)

Conclusion: According to the present study results, alternation in CPEB2 expression after treatment with Ni-Thiosemicarbazone complexes, at two concentration were effective in decrease of CPEB2 expression. Evidence showed that the Ni-Thiosemicarbazone complexes has positive potential and efficacy because the drug was ineffective in decreasing gene expression in two concentrations in 24 hours (p-value 0.001)

Keywords: Ni-Thiosemicarbazones complexes, CPEB2, GAPDH, Acute lymphoblastic leukemia

Evaluation of the effects of synthesized nano-niosomes containing Artemisia turcomanica extract on the expression of caspase3 gene in breast cancer cell lines (MCF-7) (Research Paper)

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Introduction: Nanoniosomes have been considered as carriers for targeted drug delivery in modern drug delivery systems. Considering the unique biological properties of Artemisia turcomanica plant.The aim of this study was to investigate the effects of nano- niosomes containing Artemisia turcomanica extract on the expression of caspase3 gene in breast cancer cell lines MCF-7.

Methods: In this experimental study, Artemisia turcomanica plant extract was prepared and nano-niosomes thin film was fabricated using the film method and Artemisia turcomanica plant extract was loaded with different concentrations. Physicochemical properties of nano-niosomes by SEM, FTIR and DLS approved. The cytotoxic effects nano- Niosomes containing extracts on MCF-7 cell line at concentrations of 1000, 500, 250, 125, 62.5, 31.25, 15.625Î¼g/ml were investigated by MTT method. Subsequently, also the expression of caspase 3 gene of MCF-7 cells at concentration of IC50, was investigated using Real Time PCR.

Results: The results of this study showed that the synthesized nano-niosomes containing the extract have a spherical structure and its size is less than 30-50 nm. Treatment of MCF-7 cells with nano-niosomes containing different concentrations of extracts for 24 hours at concentrations of 1000 and 500 Î¼g/ml had the highest inhibition of cell proliferation which was statistically significant (P<0.001).It was also found that the concentration of IC50 nano-niosomes containing the extract (230.56Âµg/ml.) reduces the expression of caspase 3 gene in breast cancer cell line MCF-7.

Conclusion: According to the results, it is possible that in the future, nano-niosomes can be used as a candidate drug combination for pharmaceutical purposes, but more studies are needed.

Keywords: Artemisia turcomanica, nano-niosome , Caspase 3, Breast Cancer Cell line MCF-7.

Evaluation of the Mother of Vinegar as a Potential Wound Dressing for Diabetic Wounds and its Antibacterial Properties (Research Paper)

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Introduction: Acetic acid bacteria are obligate aerobic microorganisms able to convert ethanol to acetic acid. One of the two methods for vinegar production is a traditional method. The traditional method is slow acetification carried out resulting in high-quality vinegar. It is a static method, the so-called surface culture method or Orleans method, where acetobacter is placed on the surface of the liquid, evolved into a biofilm in direct contact with oxygen. This biofilm, called â€œMother of vinegarâ€• is used as a wound dress in this study. In wounds caused by diabetes or burns, the rate of healing is low, and proper wound dressing provides the right conditions to prevent the wound from becoming infected and help improve wound healing. This wound dress with a bacterial source has nano-sized pores that prevent the passage of pathogens and contains acetic acid in its tissue, which can kill bacteria.

Methods: A total of 30 male mice were kept in the pet for a week to adapt to the environment. Mice were divided into 4 groups: healthy, diabetic wound with cellulose wound dress, negative control, and positive control. After this period, we used Streptozotocin (STZ) to create a diabetic model. After 2 days, a blood glucose test was performed and all mice became diabetic. A wound 0.9 cm in diameter was then punctured in the back of the mouse and held in place by the wound holder. Picric acid was used to protect the wound. The results were observed and recorded on days 5, 10, and 15. Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) assay were used for the antibacterial test of cellulose biofilm.

Results: The results showed that the cellulose biofilm had better results than the positive control and negative control samples, so the wound healing percentage on days 5, 10, and 15 was 40%, 80%, and 98%, respectively, but the negative control on days 5, 10 And 15 had a 14%, 34%, and 70% improvement, respectively, which showed a beneficial result of this wound dressing. On days 5, 10, and 15 no infection was seen in any of the wounds. The results of antibacterial activity showed that the effect of wound dressing on gram-negative bacteria is more than gram-positive bacteria and is related to their wall type. Inhibitory concentrations for gram-negative and gram-positive bacteria are 0.2 and 0.3 grams, respectively, and lethal concentrations for gram-negative and gram-positive bacteria are 0.3 and 0.4 grams, respectively.

Conclusion: Diabetic wound healing is one of the problems today that its repair requires a proper wound dressing. Problems with diabetic ulcers include the cost of treatment and amputation. Since in this study and similar studies, acetic acid heals wounds and due to the specific structure of this cellulose biofilm, it can be expected that this wound dressing is a suitable option for this treatment. In the results of the microbial test, this wound had the ability to inhibit and kill more gram-negative bacteria than gram-positive bacteria, and the reason for this difference, like other research, showed that differences in cell wall structure can achieve this result.

Keywords: Wound dress, Diabetes wound, Acetobacter, Cellulose biofilm, Mother of vinegar

Exploitation of two selected immunogenic proteins, OmpA and BauA, for protection against Acinetobacter baumannii infection (Research Paper)

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Introduction: Acinetobacter baumannii is a hospital opportunistic pathogen, which is a gram-negative and non-flagellated bacillus, which is considered as a common nosocomial infection with high mortality that mostly causes sepsis and meningitis. And infection of the urinary tract. Reproduction and persistence of A. baumannii in eukaryotes based on iron uptake functions including siderophore biosynthesis. Iron transfer into the cytosol is mediated by specific membrane receptors that detect iron-siderophore complexes. The expression of this Acinetobactin-mediated iron uptake system is critical for the intracellular growth of A. baumannii. OmpA is the most abundant membrane protein gram-negative bacteria and is also the major protein of bacterial pathogenesis. The production of new monoclonal antibodies against outer membrane protein A (OmpA) could be considered as a potential tool to improve the treatment of A. baumannii infections. The A. baumannii is usually resistant to beta-lactams, aminoglycosides, rifampin, and fluoroquinolones. This bacterium has led to the use of new therapies such as vaccines. No vaccine is known for this bacterium, but it is still worth considering. In this study, we used two separately selected and recombinant proteins, OmpA and BauA, as vaccine candidates to evaluate immunogenicity against A. baumannii in a mouse model.

Methods: Based on a pre-designed primer from Shahed University Bank, BauA and OmpA gene fragments were extracted from the bacterial genome PCR and the clones simulated in pet28 were expressed in Escherichia coli BL21 (DE3). The product was analyzed by SDS-PAGE method and purified by the Ni_NTA affinity chromatography method. These proteins were injected into BALB/c mice separately and in combination. The titer of IgG-specific antibody produced against each group was determined after experiment using the indirect ELISA method. Bacterial proteins were then identified by IgG immunoblotting.

Results: OmpA and BauA were already reported to raise antibodies against these proteins. The same results were obtained. The combination of the two antigens led to significant protection against A. baumannii in comparison to the single antigens.

Conclusion: Administration of the combined antigens triggers better protection than single antigens.

Keywords: Acinetobacter baumannii, Antigen, Antibody, Vaccine, OmpA, BauA.

Expression of a recombinant vaccine candidate against pathogenic strains of Shigella and evaluation of its immunity in mice (Research Paper)

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Introduction: Shigellosis, a severe diarrheal disease, is caused by pathogenic strains of Shigella. Because of the emergence of antibiotic-resistant strains of the bacteria, there is an urgent need for the development of efficient vaccines against the bacteria. However, till now, there is no approved vaccine against the disease. In the present study, the efficiency of a recombinant vaccine containing potent epitopes of seven different Shigella proteins, including seven conserved antigens of the bacteria, including IpaA, IpaB, IpaC, IpaD, OmpC, OmpF and VirG was investigated.

Methods: : The recombinant protein was expressed in E. coli expression system. Following the optimization of the expression conditions, the expressed protein was purified with gradient concentration of urea. The recombinant protein was administered to BALB/c mice in a 3 doses regimen in days 0, 21 and 35. The humoral immunity was evaluated by assessing specific IgG using enzyme-linked immunosorbent assay (ELISA). The protective immunity of the vaccine candidate is going to be investigated by intraperitoneal administration of 10 LD50 of live Shigella bacteria (This part is going to be done in next month

Results: : The protein was successfully expressed in E. coli expression system. The expression was confirmed via SDS-PAGE and Western blotting. Administration of the antigen to mice resulted in the proper stimulation of the humoral immunity. The result of the protective immunity evaluation will be obtained during the next month.

Conclusion: Our results show that this antigen is a proper candidate vaccine that can be considered a promising anti-shigellosis vaccine; however, the result of the protective immunity evaluation is needed to have a straightforward conclusion.

Keywords: Shigella; Vaccine candidate; Recombinant protein;

Fabrication and characterization of a nanocomposite bacterial cellulose based wound dressing (Research Paper)

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Introduction: Bacterial cellulose (BC) is a natural biosynthetic cellulose hydrogel, mainly produced by well-known Gluconacetobacter xylinus bacteria. BC is being widely explored for various medical applications due to its favorable characteristics such as mechanical properties, biocompatibility, biodegradability, and high moisture content. Although there are many findings on the suitability of BC hydrogel as a wound dressing, BC itself lacks antibacterial properties and is thus unable to provide a barrier against wound infection. Therefore, numerous approaches have been introduced to modify BC and optimize its antimicrobial activity. Integrating a delivery system of antimicrobial agents to BC hydrogel is a promising solution to this problem. Electrospun nanofibrous membranes are recognized as sustainable drug delivery systems, capable of loading a wide range of drugs through a variety of methods. Coating nanofibers with antibiotics is a local and temporary loading method which plays a physical role in protecting the wound, and accelerating healing process by treating infections. In this regard, here, we fabricated a composite wound dressing consisting a BC hydrogel and ciprofloxacin (CIP)-loaded polycaprolactone (PCL) nanofibrous mat to take advantage of all the distinct properties of these materials in wound healing. Nanofibrous PCL mat was chosen because it has been frequently regarded as a highly propitious carrier for loading low-molecular-weight antibacterial agents. CIP is also a fluoroquinolone antibiotic, capable of inhibiting the growth of both gram-positive and gram-negative bacteria in infectious wounds. Unique characteristics of designed nanocomposite dressing like biocompatibility and biodegradability as well as controlled release ability and antibacterial properties, make it a potential applicant for wound healing applications.

Methods: BC membrane was produced by culturing Gluconacetobacter Xylinus in Hestrin-Schramm culture mediumÙˆ including D-glucose (20g l-1), peptone (5gl-1), yeast extract (5gl-1), Na2HPO4 (2.7gl-1) and citric acid (1.15g l-1) at 30 CÂ° for 7days. Nanofibrous layer was produced by electrospinning of PCL (12%wt) in a composite solvent containing ethanol/chloroform. Immediately after electrospinning, CIP solution was electrosprayed on nanofibrous mat. Finally, CIP-PCL layer was positioned on BC hydrogel to obtain a nanocomposite wound dressing. Successful loading of CIP on PCL fibers was assessed through Attenuated Total Reflection-Fourier Transform Infrared (ATR-FTIR) spectroscopy. Subsequently, wettability and rate of water vapor movement through the samples was determined. Finally, the antibacterial

assessment study was carried out using both gram-negative (Escherichia coli or E-coli) and gram-positive (Staphylococcus aureus or S. aureus) bacteria.

Results: The ATR-IR spectrum of PCL/CIP scaffold demonstrated a characteristic peak around 1605m-1 and 3109-3155cm-1 correlated to NH group and aromatic ring of CIP, respectively. Water contact angle and rate of water vapor movement of drug-loaded dressing were measured in the range of 25-30Â° and 23-24mg/cm2.h, respectively. Antibacterial activity also indicated a clear zone of inhibition around the drug-loaded nanofibrous mat against both Gram-positive and Gram-negative bacteria, while no antibacterial activity was detected for drug-free dressing.

Conclusion: To conclude, loading and deposition of CIP on the surface of PCL nanofibrous membrane has been successfully developed and a drug-delivery system with suitable hydrophilicity and moisture permeability obtained. Composition of CIP-PCL layer and BC hydrogel resulted a modified nanocomposite dressing that exhibited significant antibacterial rates with more than 99% reduction against E. coli and S. aureus. In summary, obtained results manifest that nanocomposite CIP-PCL/BC membrane is promising for antimicrobial wound dressing with good biocompatibility to promote wound healing.

Keywords: Bacterial cellulose; Polycaprolactone; Ciprofloxacin; Wound dressing.

Fabrication and Characterization of a Novel Bacterial Cellulose/Gelatin Hydrogel Composite as a Multifunctional Scaffold in Tissue Engineering (Research Paper)

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Introduction: Fundamentally, polymeric biomaterials contain either synthetic or naturally occurring polymers. Bacterial cellulose (BC) and Gelatin, subsumed into the natural category possess such great properties as hydrophilicity, biocompatibility and biodegradability. These unique features lead to the fabrication of hydrogel composites bestowing promising vehicles upon novel fields such as tissue engineering and regenerative medicine. The in situ combination of the above-mentioned biopolymers, along with a proper cross-linking agent, yields three-dimensional (3D) porous substrate in which BC serves as a framework, and gelatin is considered as a filler. This hybrid network demonstrated outstanding physico-chemical properties including water-uptake capability as well as open and interconnected macroporosity.

Methods: BC/gelatin hydrogel was fabricated by adding 0.5 wt/v% gelatin into the BC production culture medium, containing D-glucose (100 gL-1), yeast extract (10 gL-1), peptone (5 gL-1) and CaCO3 (20 gL-1). The cultures were maintained in 28 ÂºC for 21 days under static conditions. Physico-chemical features of the hydrogels were analyzed by scanning electron microscopy (SEM), ATR-FTIR spectroscopy and X-ray diffraction (XRD). Furthermore, swelling ratio of hydrogels were assessed via a hydrolytic method based on the measurement of weight changes during 24 hours.

Results: SEM micrographs showed porous and interconnected structure of BC/gelatin composite. The ATR-FTIR spectrum of BC/gelatin depicted the stretching band at about 1530cm-1 attributed to the amide II bonds between carboxyl group of BC and amine group of gelatin. On the contrary, this band was not observed in the context of BC hydrogel. The XRD characterization of BC/Gel and BC demonstrated no significant changes in the crystalline structure. Their crystallinity index, in contrast, showed a slight difference. The swelling ratio of the BC/gelatin hydrogel in deionized water was found to reach the maximum level at 3 hours. However, in comparison with BC, the swelling ratio of the hybrid hydrogel decreased gradually within 24 hours.

Conclusion: BC/gelatin hydrogel containing porous construction, gradual biodegradability and high water absorption ability can delineate a new horizon to the innovative areas such as tissue regeneration and drug delivery systems.

Keywords: Bacterial cellulose; Gelatin; Hydrogel; Tissue engineering

Gene therapy, its limitations and risks in hemophilia (Review)

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Introduction: Hemophilia is a representative genetic disease with spontaneous bleeding caused by a loss of gene function related to the intrinsic, extrinsic, and common coagulation pathway. Gene therapy provides a potential phenotypic cure for hemophilia yet the cost of this novel treatment is high, tempering enthusiasm and raising questions regarding cost us benefit. Gene replacement therapies provide safe, durable, and stable transgene expression while avoiding the challenges of clotting factor replacement therapies in patients with hemophilia

Methods: We reviewed about 22 articles were conducted from 2016 to 2022 in the world and Iran. We searched some key words such as Gene therapy, hemophilia, AAV vectors, hepatotoxicity in sciencedirect, Elsevier, PubMed and SID.

Results: Our results showed that a fundamental treatment has yet been developed and hemophilia A and B are among the most prominent target for gene therapy. The most commonly used treatment for hemophilia is prophylaxis, wherein deficient clotting factor are supplemented depending on the type of hemophilia. A deno_associated virus (AAV) gene therapy has been clinically tested and has demon stated efficacy in restoring deficient clotting factors. Gene therapy targeting hemophilia involves intravenous administration of the F8 transgene within a viral capsid. Intravenous administration lead to preferential targeting of the transgene to the hepatocyte because of the architecture of the livers capillaries. Once the host cell identifies the AAV capsid through its glycosylated cell surface receptors, the virus is internalized via clathrin mediated endocytosis and transported in the cytosol via the cytoskeletal network. A major limitation of the AAV based gene therapy is episomal AAV genomes are not replicated during cell division. Important point to consider when using this approach are the potential loss of factor expression and the consequences of liver growth and dilution of transduced hepatocytes in younger patients. Unfortunately, repeat administration is contraindicated because after the first dose, a humoral immune response is generated against the AAV capsid proteins. It is possible, however, for the raav vector to integrate into animal genomes, which might alleviate the dilution effect. It is important to consider the potential for the development of genotoxicity, which, although rare, can occur. Difficulties removing cellular and viral impurities from raav particles as well as empty AAV capsids, lack of stander dilation, and inherent batch to batch variation in vector potency affect production cost. The availability of convincing evidence for long term expression of transgenic FV Ð¨ and F Ð†Ò³ at therapeutic levels, resulting in amelioration of the bleeding diathesis following AAV.

Conclusion: According to the results, mediated gene transfer is an important step toward development of curative gene therapy. Several obstacles still remain, but the field is evolving at a rapid pace, raising the prospects of eventual license of gene therapy for the hemophilia. Such a product would change the treatment paradigm for patients with severe hemophilia and facilitate the development of gene therapy for other monogenetic disorders, particular those with limited or non-existed treatment options.

Keywords: Gene therapy, hemophilia, AAV vectors, hepatotoxicity, limitations

Generation HIF-1Î± knockout of MKN45 gastric cancer cell line by CRISPR CAS9 system (Research Paper)

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Introduction: Today, the knockout cell line can accelerate cancer research by providing a model for evaluating tumorigenic mechanisms, studying cancer cell drug resistance, identifying drug development targets and assessing cell therapy. Hypoxia is an in common feature of solid tumor microenvironment especially at its core site. This chronic hypoxia resulted in the development of resistance to drug and apoptosis, elevated angiogenesis and metastasis. Hypoxia-Inducible Factor (HIF)-1 plays a critical role in the response to low oxygen concentration in tumor cells, so it may be a viable candidate for use in the development of knock-out cells for cancer research. Thus, in the present study, HIF-1Î± knock-out was introduced to the human gastric cancer MKN45 cells using a lentivirus-mediated CRISPR/Cas9 system (TLCV2-Cas9).

Methods: The target HIF-1Î± sgRNA was initially designed and cloned into the TLCV2-Cas9 plasmid and confirmed by sequencing. Then, the resulted plasmid was transected into the human epithelial cell line HEK-293. The virus particles were harvested and used for transduction of MKN45 cells. After puromycin selection, genomic DNA was analyzed using the T7E1 for evaluating knock-out induction. clonal selection was performed to reach a pure knock-out clones and validated by sequencing.

Results: The TLCV2-Cas9 plasmid was constructed correctly based on the results of the sequencing. The HEK-293 cell line was successfully transfected with the plasmid that was obtained. The MKN45 cells were also infected with viral particles. The T7E1 test results demonstrate that the knockout induction was successfully completed. Finally, the sequencing results validated the creation of a pure knockout cell clone and the HIF-1Î± gene was successfully knocked out in MKN45 gastric cancer cells.

Conclusion: As a result of this research, a gastric cancer cell model that can be used for therapeutic purposes was created using the CRISPR CAS9 technology.

Keywords: CRISPR/Cas9 system, Gastric cancer, HIF-1Î±, knockout cell lines

Genetic factors associated with increased severity of Covidâ€• 19 (Review)

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Introduction: Covid19 is the third most aggressive coronavirus that spreads rapidly and kills many people. It is a multigenic and multifactorial disease with many genetic and environmental determinants. The present review gives a brief overview of different genes involved in the infection by SARS-CoV-2 and its association with disease severity.

Methods: searching review studies including this field in web browser

Results: Several studies indicated that the genetic variants of the SARSâ€□CoVâ€□2 entry mechanismâ€□related (angiotensinâ€□converting enzymes, transmembrane serine proteaseâ€• 2, furin) and host innate immune responseâ€• related genes (interferons [IFNs], interleukins, tollâ€• like receptors), and human leukocyte antigen, ABO, 3p21.31, and 9q34.2 loci are significantly related to Covidâ€• 19 severity. 1- ANGIOTENSINâ€□CONVERTING ENZYMES Angiotensin Iâ€□converting enzyme (ACE) and angiotensinâ€□converting enzymeâ€□2 (ACE2) are homolog genes that regulate physiological homeostasis of reninâ€“angiotensin system (RAS). SARSâ€□CoVâ€□2 uses the ACE2 receptors to invade the target cells. Transcriptome analyses of 700 lung samples revealed that ACE2 was highly expressed in severe patients, compared with controls, and comorbidities may lead to higher chances of developing severe Covidâ€• 19. On the contrary, some reports have indicated a negative correlation between ACE2 expression and Covidâ€• 19 severity. 2- GENETIC VARIANTS OF CELLULAR PROTEASES Transmembrane serine proteaseâ€• 2: TMPRSS2 gene encodes a serine protease enzyme that is involved in cleavage and activation of the SARSâ€□CoVâ€□2 spike protein during membrane fusion. it was suggested that genotyping studies of Covidâ€• 19 patients could aid in understanding the impact of TMPRSS2 variations on clinical outcomes. Furin: SARSâ€□CoVâ€□2 spike protein contains a multibasic S1/S2 site where host cell protease Furin can cleave S protein Furin is essential for proteolytic activation of SARSâ€□CoVâ€□2, so inhibition of this protease ensures a therapeutic approach for treatment of Covidâ€• 19. 3- GENETIC VARIATIONS OF IMMUNITY COMPONENTS Interferons: for example IFNAR1 and IFNAR2 are a family of specialized cytokines that activate a cell signaling cascade, controlling the induction of hundreds of interferonâ€• stimulated genes. Three distinct types of IFNs, Types I, II, and III, mediate antiviral response and activate host defence against viral infections. Interleukins (ILs): ILâ€• 1 signaling pathway component TMEM189â€“UBE2V1 was the most significant gene locus associated with severity. IL6 is a pro-inflammatory cytokine The overexpression of this cytokine was associated with increased COVID-19 risk and death. Tollâ€• like receptors (TLRs): TLRs are a family of innate immune receptor

molecules known as pattern recognition receptors (PRRs). TLR3 is the most widely expressed TLR that recognizes virusâ€□ derived doubleâ€□stranded (ds) sRNA. 4- HLA LOCUS The HLA region consists of more than 240 genes and they are divided into three classes, namely I, II, and III. The HLA system consists of a group of proteins that play a crucial role in the antigen presentation and genetic diversity. HLA is the most polymorphic genetic locus in human. The frequencies of the HLAâ€• C*07:29 and B*15:27 alleles were significantly higher in Covidâ€• 19 patients. 5- 3P21.31 AND 9Q34.2 LOCI Genome wide association study(GWAS) of severe Covidâ€• 19 with respiratory failure revealed a significant association with rs11385942 at locus 3p21.31 and with rs657152 at locus 9q34.2. CXCL16 and CXCR6 SLC6A20 are genes are within the 3p21.31 locus. Two GWAS of severe Covidâ€• 19 reported that blood group A shows higher risk than other blood groups, whereas O group displays a protective effect as compared with other blood groups. 6- APOLIPOPROTEINS Apolipoprotein E (APOE) is a polymorphic gene locus and Îµ2/Îµ3/Îµ4 alleles code for three major isoforms in plasma.It was found that individuals homozygous for APOE4 were more likely to be positive for Covidâ€• 19, and thus severe disease. 7- OTHER GENES DPP9 locus was also associated with severe Covidâ€□19 in a GWAS and the COVIDâ€□19 HGI report. Researches identified four missense and one intronic noncoding variant in four genes ERAP2 (rs150892504), BRF2 (rs138763430), TMEM181 (rs117665206), and ALOXE3 (rs147149459 and rs151256885) that significantly increase risk of death in Covidâ€• 19 patients.

Conclusion: Identifying genetic markers associated with the susceptibility or clinical outcome of COVID-19 could provide an essential contribution to the knowledge of this disease for the detection of susceptible individuals or populations and the design of therapeutic strategies (i.e., vaccine and pharmacologic treatment).

Keywords: COVID-19, Genetic variants, SARS-CoV-2, Polymorphism, Severity and mortality

GGDPS is a key enzyme in the steviol glycosides biosynthesis pathway (Research Paper)

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Introduction: Diterpenoid steviol glycosides are sugar compounds extracted from Stevia rebaudiana Bertoni which belongs to Asteraceae family. Stevioside and rebaudiosideA make the most of sugars in this plant. Steviol glycosides biosynthetic pathways share four steps in common with gibberellic acid formation. Steviol was synthesized from kaurene via the mevalonate (MEP) pathway. Kaurenoic acid 13-hydroxylase (KAH) is the first specific enzyme in the steviol glycosides biosynthesis pathway.

Methods: The accession numbers of genes involved in the steviol glycosides biosynthesis and their protein IDs were downloaded from the literature and the National Center for Biotechnology Information (NCBI) database (https://www.ncbi.nlm.nih.gov/). The sequences were aligned using the ClustalW in Bioedit sequence alignment editor tool version 7.0.9.0. Dendrogram trees were drawed using Molecular Evolutionary Genetics Analysis (MEGA) 5.2.2 software. The neighbor-joining (NJ) method was used to construct a phylogenetic tree.

Results: The results showed S. rebaudiana , Helianthus annuus, Lactuca sativa, and Artemisia annua are most similar in evolution GGDPS gene is only found in S. rebaudiana, therefore this gene is specific to this plant.

Conclusion: GGDPS is a key enzyme in the steviol glycosides biosynthesis pathway. It seems that geranylgeranyl diphosphate in the evolution has become geranylgeranyl pyrophosphate synthase. It is because the amount of gibberellin produced in the other plants is much less than the amount of steviol glycosides.

Keywords: Stevia rebaudiana, steviol glycosides, GGDPS, biosynthesis pathway, phylogenetic tree

Green synthesis of silver nanoparticles with different sizes and investigation of size-dependent antibacterial activity (Research Paper)

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Introduction: Introduction & Aim: Nanotechnology is a modern research field about synthesis, modification, properties and usage of particles ranging from 1 to 100nm in size. Novel applications of nanoparticles and nanomaterials are developing rapidly in many areas, such as healthcare, cosmetics, biomedical, food, drug/gene delivery, environment, health, mechanics, optics, and chemical industries and etc. Currently, research regarding the interaction between nanoparticles and biomedicine is increasing, and as a result, a wide variety of inorganic nanoparticles are used for biological applications. Green synthesis of nanoparticles, as an emerging highlight of the intersection of nanotechnology and biotechnology, was attractive due to the growing need to develop environmentally benign technologies in material synthesis. The techniques for obtaining nanoparticles using naturally occurring reagents such as sugars, biodegradable polymers (chitosan, etc.), plant extracts, and microorganisms as reducing and capping agents could be considered attractive for nanotechnology. Eugenol, the main constituent of essential oils extracted from various plants, has been widely studied due to its medicinal properties, such as its antibacterial effect. Similarly, silver nanoparticles have been extensively investigated because of their antimicrobial properties alone or in combination with other compounds. In this study, different sizes of silver nanoparticles were synthesized with eugenol to compare the antibacterial effect of each nanoparticle.

Methods: Methods: Ag nanoparticles (AgNPs) were synthesized with four different concentrations of eugenol. We prepare eugenol 10, 40, 70, 100Î¼M eugenol in 2ml ethanol and also 20mM AgNO3 solution was prepared with 10ml distillated water. 2ml of AgNO3 solution was mixed with 46ml deionized water in each 4 dishes on the stirrer. Then we added 2ml of each concentration of eugenol to the solutions. By reaching the pH of the solution to 11, we saw the color of the solution change from colorless to blackish brown. Then we Placed the solution on the stirrer for one hour at room temperature (1000rpm). Thereafter, a blackish brownâ€• colored mixture was centrifuged for 20min (4000rpm) and the nanoparticles was used. Nanoparticles was assessed through dynamic light scattering and ultraviolet-visible spectroscopy. We use Escherichia coli to determine the MIC of each nanoparticle. For MIC test, different concentrations of nanoparticles (100, 150, 200, 300, 400, 500Î¼g/Î¼l) were prepared. Also, we prepared E. coli standard solution (include 1.5 Ã— 108 bacteria). The MIC test was performed on 96-well plates. Three columns of plate were considered for Each nanoparticle. each concentration of nanoparticles was added in three well in each row with 20Î¼l bacteria. Also, two rows were considered as positive control and negative control. Samples

were incubated for 24 hours and then MIC was detected by bacterial turbidity in the wells.

Results: Results: The UV-Vis results show peaks of all four samples were around 400 nm, which is a characteristic value for spherical silver nanoparticles, we have different absorbance for each nanoparticle, the nanoparticle made with eugenol 10Î¼M have more absorbance than the other one. Also, the nanoparticle made with eugenol 10,40Î¼M have darker than the other solutions. The DLS graphic of AgNPs showed different size of nanoparticle based on eugenol molarity. The largest nanoparticle was made with eugenol 10Î¼M with a size of 512 nm and also the smallest synthesized nanoparticle was the nanoparticle made with eugenol 100Î¼M with a size of 226nm. The size of nanoparticles made with eugenol 40, 70Î¼M was 500 and 239, respectively. with an increasing concentration of eugenol, the size of the nanoparticles became smaller. The MIC of each sample was determined according to the degree of bacterial turbidity in each well compared to the negative control. MIC obtained from nanoparticles made with eugenol 10,40,70,100Î¼M against E. coli was 100,150,400,400Î¼M, respectively.

Conclusion: Conclusion: Our results revealed an association between the eugenol concentration for Ag nanoparticles synthesized and nanoparticles size. The reverse association was seen in Ag nanoparticles size and antibacterial effect. These findings lead to the conclusion that aiming for the smallest possible nanoparticles might not be the best course of action, despite the general standpoint of the relevant literature.

Keywords: Key words: nanoparticle size, silver nanoparticle, eugenol, antimicrobial effect

Growth and effectiveness of the Arugula (Eruca vesicaria) in the outdoor hydroponic system. (Research Paper)

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Introduction: Nowadays, under the influence of rapid population growth, land desertification, and climate change, many agricultural problems have begun to appear. Hydroponics as a new field of biological industry, modern biotechnological method to obtain raw materials, provides optimal conditions for plant growth and through advanced conditions, more efficient raw materials, high quality and ecologically clean to gains.In recent years, the Institute of Hydroponics at the National Academy of Sciences of Armenia has conducted numerous studies on the quality and effect of Davtyan nutrient solution on the growth, development and efficiency of a variety of useful and valuable vegetables, including Arugula (Eruca vesicaria).

Methods: The experiments were carried out in self-nourishing hydroponic equipments (with the density of 70 plants/m2), using EBB & Flow hydroponic system. A mixture of volcanic slag + gravel in 1:1 ratio with the 3-15 mm diameter particles was used as a substrate. The plants nourishment were done with different concentrations (0.5 N, 0.75 N, 1.0 N 1.25 N) of Davtyanâ€™s nutrient solution. Arugula is early-ripening (35-40 days), so the experiments were carried out twice during the vegetation: in spring - in April and in summer - in August. Ordinary soil culture served as a control. During the vegetation biometric measurements and a number of biochemical-physiological analyzes have been done. The content of vitamin C in the plant raw material was determined according to Yermakov, the content of Î² carotene has been estimated according to Sapozhnikov, extractive substances according to State Pharmacopoeia and the total content of flavonoids according to Georgysky.

Results: The results of research showed that in hydroponic culture the relatively high yield (1.1-1.2 times) of arugula in the first and second growing season was observed at a concentration of 1.0 N of nutrient solution. And the cultivation of the soil by the mentioned indicator was inferior to other hydroponic variants in period I - by 1,2-1,4 times and in period II - by 1,1-1,3 times.. Higher

content of vitamin C in plant raw materials was observed in the first (1.4-2.4 and 1.6-2.9 times) and second (1.3-1.8 and 1.5-2.4 times) periods at 1.0 N concentration of nutrient solution. At the same time, high content (1.4-1.6 times) and output (1.6-2.4 times) of Î²-carotene was also observed under 1.0 N concentration of nutrient solution.

Conclusion: During both growing season the relatively high yield of arugula and the high content of vitamin C and Î²-carotene were observed at 1.0 N concentration of nutrient solution and at soil culture.

Keywords: hydroponics, arugula, vitamin C, Î²-carotene, biotechnology

Human T-Cell Lymphotropic Virus (HTLV-1) infection in the Afghanistan: Review of a forgotten epidemic (Review)

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Introduction: Background: The distribution of HTLV affects nearly 7 million people around the world. The prevalence of this infection varies among different geographic regions as well as populations. Objective: The objective of this revue was to present the epidemiological data of HTLV infection in the Afghanistan

Methods: This revue consisted in cataloging various studies, published articles and summaries presented in scientific conference having as subject of interest the HTLV in the Afghanistan. The search was done using MEDLINE/PubMed, Embase (Via Ovid), Cochrane, Google scholar, and POPLINE. To identify the articles from the different sources, the search was carried out using the following keywords: -HTLV, HTLV infection, HTLV epidemiology, kabul, Afghanistan-. Publications were selected according to the relevance of the methodology as well as the results and the representativeness of the samples

Results: In 2010 and 2011, conducted a study in the city of kabul on 32 patients screened for chronic symmetrical spastic paraparesis of which 25 (96%) had anti-HTLV-1 markers in their serum. was 102 sera samples collected in 2002 from a population of kabul , 14 (13.7%) were positive for HTLV-2. a study in kabul in 2003 and 2 on 1162 patients, 36 (3.1%) were positive for anti-HTLV-1 markers.

Conclusion: This analysis shows that HTLV infection was of interest and has lost interest today. Its prevalence in this decade was between 1% and 15% in the Afghanistan. It was higher than that of HIV during the same period.

Keywords: HTLV, Infection, Epidemiology, Afghanistan

Hybridoma technology, a highly efficient method for the production of monoclonal antibodies (Review)

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Introduction: It's not a new concept to use someone's blood who has recovered from an illness to assist another person recover from the same illness. During the 1918 influenza virus pandemic, doctors would use serum from persons who had recovered from the disease and give it to those who were infected to prevent the disease from progressing. Antibodies generated by the immune system to detect and eradicate infections were thought to be present in this blood. We can now extract and create particular antibodies to treat a range of diseases thanks to scientific advancements over the last 30 years. This group of antibodies is called monoclonal antibodies (mAbs). mAbs are lab-made proteins that mimic human antibodies by attaching to antigens, which are specific proteins found in the body. Proteins from tumors, bacteria, viruses, and inflammatory cells are examples of antigens. Currently, approximately 30 monoclonal antibodies have been approved for use in medicine to treat a variety of disorders. Human monoclonal antibodies, in particular, are currently on the list of targeted therapeutics for Covid-19. One of the most frequent methods for producing mAbs is hybridoma technology. After immunizing mice with specific antigens, antibody-producing B lymphocytes are separated and united with immortal myeloma cell lines to create hybrid cells known as hybridoma cell lines. In a laboratory, these hybridoma cells are cultivated to create monoclonal antibodies against a specific antigen.

Methods: We conducted a thorough search in online databases such as Google Scholar, Web of Science, PubMed, and Scopus to find all articles related to Hybridoma technology for the production of monoclonal antibodies published from 2018 until 2022. We conducted no language limit and our search strategies for each database were independently designed. Our studies included all observational conducted to explain the applications of monoclonal antibodies in medical and diagnostic matters, and a special and complete review of hybridoma technology for the production of mAbs. Through screening the abstracts/titles of the articles we selected the relevant studies. Duplicate and Similar searches were excluded and the references of the extracted publications were reviewed to ensure that all relevant studies were included.

Results: Hybridoma technology has long been regarded as a wonderful and necessary tool for producing high-quality monoclonal antibodies (mAbs). Hybridoma-derived mAbs have become the most quickly expanding class of therapeutic biologics, not only as tool reagents but also as therapeutic biologics. Hybridoma technology has opened up new options for effectively producing

humanized or fully human mAbs as treatments, with the establishment of mAb humanization and the production of transgenic-humanized mice. The hybridoma method takes advantage of mature B lymphocytes found in the secondary lymphoid organ, which are produced in response to an invading antigen. The variable area of antibodies in these B cells in the secondary lymphoid organ expands as a result of accumulating corporeal hypermutations, resulting in the selection of high-affinity binder antibodies. These antibodies have the ability to naturally link substantial and light chain genes. A well-known method for manufacturing monoclonal antibodies is to fuse vaccinated mice's splenocytes with immortal myeloma cells to form hybridoma cell lines. Despite the fact that other technologies for the creation of monoclonal antibodies have emerged as feasible alternatives, hybridoma technology remains a viable technique that is accessible to a wide range of laboratories that do basic cell biology research.

Conclusion: Cell biology, immunology, biotechnology, toxicology, pharmaceutical and medical research have all benefited from hybridoma technology. Prior to the invention of hybridoma technology, antibodies were made by immunizing laboratory animals and then isolating the serum, which could subsequently be used for medicinal purposes. However, those procedures have a number of drawbacks, including the possibility of allergic and hypersensitive reactions in patients. Furthermore, no clinical trials for the administration of crude sera were conducted. Hybridoma technology ushered in a paradigm change by allowing for the mass manufacture of extremely specific and sensitive monoclonal antibodies. The mAbs have been employed in a variety of diagnostic applications, including cancer detection. These are also widely utilized in cancer treatment. Fusion of antigen-specific human B-cells with human or mouse metastatic tumor cells is the most cost-effective and efficient way of producing antibodies. Researchers are working ceaselessly in the current biotherapeutic era to generate simpler and higher-quality human antibodies with the help of hybridoma technology.

Keywords: Hybridoma technology, Monoclonal antibody, Therapeutic, B cells, Diagnosis

Identification of a new deleterious single nucleotide polymorphism related to CDKN3 gene in colorectal cancer by bioinformatics analysis (Review)

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Introduction: Introduction: Colorectal cancer (CRC) is the third most popular occurring cancer in men and the second most commonly occurring cancer in women. It is a disease originating from the epithelial cells lining the colon or rectum of the gastrointestinal tract. CRC is more likely to be due to old age and lifestyle factors, and a small number of people become infected due to mutations in intestinal crypt stem cells [1]. Signs and symptoms may include blood in the stool, a change in bowel movements, weight loss, and fatigue. It typically starts as a benign tumor [2]. CDKN3 gene is located position on chromosome 14q22.2 and contains 9 exons. Different studies indicated that this gene is associated with CRC. Cyclin-dependent kinase inhibitor 3 (CDKN3) is a member of the protein kinase family with KrÃ¼ppel-associated box repression domains that have synergistic and inhibitory effects on zinc finger proteins. CDKN3 plays a dual role in cell cycle control, either blocking or promoting cell cycle progression in specific tumors or tumor stages [3]. Single nucleotide polymorphism (SNPs) are consisting genetic marker related to many of the genetic diseases that variation at a single position in a DNA sequence among individuals that this particular alteration is made in at least 1% of the population [4]. Given the importance of SNPs as biological markers of cancer, this study aimed to investigate new deleterious SNPs related to CDKN3 gene in CRC by bioinformatics analysis.

Methods: Methods: In this study, NCBI, PROVEAN, SIFT, and HOPE online bioinformatics webservers were used for evaluation of new deleterious SNPs in CDKN3 gene and their effects of its protein in CRC.

Results: Results: We detected several SNPs in the protein coding region of CDKN3 gene. From all of the extracted SNPs, rs78293998 introduced as the most significant deleterious SNP in the protein-coding region of CDKN3 gene. Our bioinformatics analysis indicated that rs78293998 is associated to the substitution of the reference (wild) A allele with the alternative (mutant) G allele in the CDKN3 gene. Based on the biophysical validation of HOPE, this SNP is cause the arginine mutation into Isoleucine at the 72nd position of CDKN3 protein. The wild-type and mutant amino acids differ in size. Also, the mutant residue is smaller and this might lead to loss of interactions, therefore this mutation is probably damaging to the protein

Conclusion: Conclusion: In general, we conclude that rs78293998 is associated with CDKN3 gene and CRC. Moreover, the formation of rs78293998

may increase the incidence of CRC by changing the structure of the CDKN3 protein. However, experimental studies are needed to validate the result of this in silico study.

Keywords: Keywords: Colorectal cancer, CDKN3 gene, SNPs, Bioinformatics analysis, rs78293998

Identification of LncRNA expression signatures for triple negative breast cancer by bioinformatics analysis (Research Paper)

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Introduction: Triple-negative breast cancer (TNBC) is a typical molecular subtype of breast cancer that lacks the expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) and accounts for 10-20% of all types of breast cancer (1,2). Currently, no specific targeted therapy is available for TNBC (3). Therefore, it is crucial to identify potential biomarkers and novel therapeutic targets to develop a more efficient treatment. Emerging evidence has indicated that long non-coding RNAs (lncRNAs) play a vital role in various biological processes, including genetic transcription, chromosome modification, cell differentiation, and migration (4-6).lncRNA breast cancer antiestrogen resistance 4 (BCAR4) produces a spliced long non-coding RNA (lncRNA) that has been implicated in breast cancer metastasis. It was originally identified in a screen for genes responsible for developing resistance to antiestrogens in breast cancer cells. It is thought that the release of CCL21 enables this lncRNA to bind to the SNIP1 and PNUTS transcription factors, thereby activating a non-canonical GLI-dependent hedgehog signaling pathway that promotes cancer cell migration and invasion(7). The present study searched published microarray and sequencing data in the Gene Expression Omnibus (GEO). A sample size of patients with TNBC to identify candidate RNA signatures in TNBC that BCAR4 involves TNBCâ€‘specific RNAs. These integrated analyses aimed to detect novel lncRNA/miRNA/mRNA biomarkers of TNBC and reveal the underlying molecular regulatory mechanisms of TNBC pathogenesis and progression.

Methods: Focusing on bioinformatics aspects, Data mining and Microarray datasets, including GSE38959 (8), GSE61723 (9), GSE61724 (9), GSE76250 (10), and one dataset obtained by expression profiling via high-throughput sequencing, namely GSE58135 (11), were downloaded from the GEO database (https://www.ncbi.nlm.nih.gov/geo/) and the cancer genome atlas database. NCBI obtain some information about BC to determine the chromosomal profile of BCAR4 and target genes. The LncRNA and disease database helped find diseases associated with BCAR4 (BCAR4) expressed in 27% of primary breast tumors. Forced expression of BCAR4 in human ZR-75-1 and MCF7 breast cancer cells resulted in cell proliferation in the absence of estrogen and the presence of various antiestrogens. BCAR4 may be a good target for treating antiestrogen-resistant breast cancer). The Genomic Locations for BCAR4 Gene found in GENECARD, and Latest Assembly

showed in chr16:11,808,312-11,828,905, and its expression levels in different organs (both tumor and normal state) evaluated in the GEPIA2 database.

Results: RNA sequencing data analysis between patients with breast cancer and healthy individuals showed valuable results. The result of these studies was identified that about 29% of BC patients expressed BCAR4. Patients with high expression of BCAR4 had short progression-free survival (PFS), distant metastasis-free survival (MFS), and overall survival (OS). In addition, research on molecular mechanisms found that BCAR4 activated a noncanonical Hedgehog/GLI2 signal pathway and promoted cells migration [12]. As about 70% of BC patients are estrogen receptor-positive, antiestrogen therapy is considered an effective treatment. However, resistance has already been the main challenge for antiestrogen therapy. BCAR4 is one of the critical genes related to antiestrogen resistance [13]. It is found that overexpression of BCAR4 promoted BC cells growth through a non-estrogen-dependent pathway [13]. After overexpressing BCAR4, BC cells turned sensitive into resistant to antiestrogen [14].

Conclusion: In this study, we found the critical gene (BCAR4) that performs an oncogene role in Breast cancer. The high expression level of BCAR4 indicates a poor prognosis for BC patients that can be a candidate target for diagnostic, therapeutic, and preventive purposes.

Keywords: Triple-negative breast cancer, lncRNAs, BCAR4, GEO database

Identification of mutual altered gene expression in 5 types of cancer as a target gene and potential oncogene (Research Paper)

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Introduction: Studies have shown that cancer in developed and developing countries is the first and second leading cause of death respectively. Some factors have an important role in cancer development and lead to metastasis by destroying normal cells. In the current study, we identified commonalities in gene expression among 5 types of cancer, such as rectum, colon, breast, liver, and lung.

Methods: In our study, we utilized TCGA data to identify expression profiling of the genes among the 5 cancers. For this purpose oncoDB (http://oncodb.org/) was used and raw gene-level read counts were normalized using the transcripts per million (TPM) method. For comparative analysis of cancer samples and normal samples, we obtained gene expression from The Cancer Genome Atlas (TCGA) for all 5 types of cancer. Moreover, we used an interactivevenn (http://www.interactivenn.net/) to identify the commonality of genes associated with these 5 types of cancers.

Results: The results of differential expression analysis between cancer samples and normal samples showed some altered gene expression. A p-value of <0.05 and |log2FC |>1 was regarded as statistically significant. 19 mutual genes from the 5 types of cancers were selected and 15 of 19 genes were overexpressed and led to tumorigenesis. Furthermore, we proposed that the majority of these genes overexpression induce tumor proliferation in tumor cells by regulating cell-cycle at the G2/M phase. Genes were such as MMP11, CTHRC1, SPP1, TRIP13, ANLN, IQGAP3, ORC6, RECQL4, UBE2C, TPX2, TROAP, NUF2, MYBL2, CENPF and CDC6.

Conclusion: Upon evaluation, our results indicate that there are 15 mutual genes associated with rectum, colon, breast, liver, and lung cancers and demonstrated a significant correlation with the expression of genes and progression of cancer. We can consider the overexpression of these 15 genes as an effective factor in the transformation of normal tissue into cancer tissue. Furthermore, these known genes not only have a special role in the progression of cancer but can also be useful for targeted therapy.

Keywords: Pan-cancer analysis,Cancer, TCGA, Gene expression, Oncogene

Immunogenicity of the combination of two outer membrane proteins, Oma 87 and BauA against Acinetobacter baumannii infection in a murine model (Research Paper)

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Introduction: Acinetobacter baumannii is a non-motile multiform pleomorphic Gramnegative cocco bacillus.Acinetobacter baumannii is a mortal nosocomial pathogen. Resistant to disinfectants, desiccation, and biofilm formation on the abiotic surfaces, and desiccation make A. baumannii as a prosperous successful pathogen in hospital environments. Acinetobacter baumannii has happen become a tremendous challenge to late modern healthcare system healthcare as an antimicrobial resistant. Outer membrane proteins (OMPs) of gram-negative bacteria are known as powerful strong immunogens. Siderophore molecules and Iron-Regulated Outer Membrane Proteins (IROMPs) are the two necessary essential members of iron attainment acquisition system. Siderophores are secreted by bacteria to stick bind circumferential peripheral ferric iron and the IROMPs are expressed at the bacterial outer membrane as the receptor of ferric-siderophore assembled complex.

Methods: BauA is the corresponding siderophore receptor of A. baumannii. In addition to antibacterial and opsonizing activity, monoclonal antibodies produced against IROMP can also block the in vitro iron absorption system. Antibodies against BauA functional regions can potentially block its functions and lead to impaired iron absorption. Therefore, it makes sense to use bioinformatics tools to select the appropriate area (s) as a vaccine candidate (s). Oma87 has been stated introduced as an immunogenic outer membrane protein per via contrary reverse vaccinology. The going current investigation research undertakes a perusal study on the immunogenicity of recombinant Oma87 in a murine sample model. BAM(Oma87) proteins are another essential OMP. The Î²-Barrel assembling machine (BAM) creates a multi-protein complex on the outer membrane of gram-negative bacteria that is involved in targeting and folding Î²-Barrel outer membrane proteins. BamA bears no resemblance to the human and mouse proteome, which is essential for inhibiting autoimmune responses in the host .Active and inactivated vaccination are considered as options for screening against the pathogen A. baumannii. . In this study, both Oma87 and BauA proteins were cloned into the plasmid pET28a. After purification, they were injected in combination to create immunity in mice. After that, the level of IgG in them was evaluated by ELISA method and the established safety was evaluated.

Results: . In this study, both Oma87 and BauA proteins were cloned into the plasmid pET28a. After purification, they were injected in combination to create immunity in mice. After that, the level of IgG in them was evaluated by ELISA

method and the established safety was evaluated. Oma87 and BauA were already repotted to raise antibodies against these proteins.

Conclusion: The same results were obtained. The combination of the two antigens led to significant protection against A.baumannii in comparison to the single antigens. As a result, the administration of combination antigens provides better protection than individual antigens.

Keywords: Acinetobacter baumannii,, Vaccine, Oma87, BauA

Importance and Mechanism of Nanoparticles in Overcoming Drug Resistance in Cancer (Review)

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Introduction: Cancer is the second biggest cause of mortality worldwide and one of the most serious public health issues. Surgery, chemotherapy, radiation therapy, targeted therapy, immunotherapy, and hormone therapy are all examples of traditional cancer treatment methods. Nanoparticles (NPs) are scientifically defined as particles having one dimension less than 100 nm that have unique qualities not present in bulk samples of the same substance. Organic NPs, inorganic NPs, and hybrid NPs are all commonly employed in drug delivery systems. By delivering small molecules for cancer detection, diagnosis, and therapy, nanotechnology has ushered in a potential new era of cancer treatment. Cancer therapies based on the unique characteristics of NPs are widely used in the therapeutic setting for a variety of cancer types. The purpose of this review article is to investigate the importance and mechanism of NPs in overcoming drug resistance in cancer.

Methods: This study looked into the role of NPs in overcoming drug resistance in cancer, and it used scientific databases including Science Direct, Springer, Google Scholar, and PubMed.

Results: The results showed the role of NPs in drug resistance overcoming one of the most serious issues in cancer treatment and management is drug resistance. It is present in all types of cancer and all therapeutic options. When diseases develop resistance to pharmaceutical therapies, this is known as drug resistance. There are two types of drug resistance: 1) intrinsic and 2) acquired. Pre-existing mutations in genes involved in cell proliferation or death are the most common cause of innate resistance. Acquired resistance in the form of resistance that develops after specific anti-tumor treatment, and can be caused by the emergence of additional mutations or changes in the TME during treatment. Nanoparticles can also be employed to combat cancer-related treatment resistance because of their amazing ability to co-encapsulate several therapeutic molecules.

Conclusion: In conclusion, NPs are an ideal platform for combination therapy, which aids in the treatment of MDR infections. Several forms of NPs, such as polymeric NPs, metallic NPs, and hybrid NPs, have shown better drug delivery efficacy as a result of increased research. Researchers must pay close attention to the qualities of therapeutic medicines as well as the attributes of the nominated nanoplatforms. More NP-based therapies can be used as proteomics research on the "mechanism of cancer origin, MDR, incidence" growing. Only a few NP-based medications are in use, a few more are in clinical trials, and the most are still in the exploratory stage, despite the massive amount of research. More effort should be put into "understanding toxicity,

cellular and physiological parameters that influence NP-based medication administration, EPR, and PC mechanism" in the human body for rational nanotechnology design. Based on the information presented above, we believe that nanotechnology and cancer therapy development will lead to a revolution in clinical translation for NP-based cancer therapy.

Keywords: Nanoparticles, cancer, Drug Resistance, Nanoplatforms

Importance of Nanoparticles in Immunotherapy in Cancer (Review)

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Introduction: Cancer is a deadly disease that affects people all around the world. Traditional cancer treatments such as chemotherapy and radiotherapy have limited therapeutic efficacy and are linked with severe side effects and a high risk of recurrence. Immunotherapeutic drugs have recently shown encouraging outcomes in clinical cancer treatment, attracting the interest of doctors and cancer patients all around the world. Cancer immunotherapy has recently become the gold standard for cancer treatment. Immunotherapy not only heals primary tumors but also inhibits metastasis and recurrence, which is a significant benefit over traditional cancer treatments. Existing cancer immunotherapies, on the other hand, have limited therapeutic benefits because tumor antigens are frequently not properly transmitted to immune cells. Solid tumors also elude anti-cancer immunity, unlike lymphoma, by creating an immune-suppressive tumor microenvironment (TME). Nanoparticles made of biomaterials are one method for circumventing cancer immunotherapy's limits. This study aimed to investigate the importance of nanoparticles in immunotherapy in cancer.

Methods: This study was conducted on the subject of the Nanoparticles in Immunotherapy in cancer to review abstract the importance and practice of modern therapies in biotechnology and by collecting content from Science Direct, Springer, Google Scholar, and PubMed sites.

Results: The results demonstrated that nanoparticles based on biomaterials improved anti-cancer immunity. Nanoparticles can carry cancer antigens and adjuvants to APCs in lymph nodes, enhancing antigen presentation. Recently developed mRNA-based neo-antigens have the advantage of low immunogenicity while still being able to mount an effective T-cell response when translated into the cytoplasm. However, such agents are susceptible to degradation by ubiquitous nucleases in the blood and are difficult to deliver into APCs. The use of nanoparticles to deliver mRNA neo-antigens to immune cells is a promising method. Nanoparticles can also aid in the re-establishment of immune surveillance by delivering immunomodulatory drugs to the TME. Drugs could be delivered to tumor tissues with high efficiency using intelligent, stimulus-responsive nanoparticles that detect the TME. Previously, the majority of nanoparticle-based cancer immunotherapeutics were administered systemically, making it difficult to avoid systemic toxicity due to large drug dosages. As a result, local cancer immunotherapy in combination with classic intentional oncology techniques holds potential for successful cancer immunotherapy since it can reduce systemic toxicity while increasing therapeutic efficacy by targeting immunotherapeutics to the solid tumor or immune system. Also, by pre-screening individuals who are particularly receptive to cancer immunotherapy, image-guided techniques could improve the success rate of cancer treatment. Artificial APCs (aAPCs) have recently

been developed. as prospective cancer immunotherapy, technology aAPCs made from micro- or nanoparticles can operate like natural APCs, activating the adaptive immune system response to cancer.

Conclusion: As a result, detailed research and understanding of the interactions between biomaterials and the immune system are required for the development of anti-cancer immunotherapy nanomaterials. The use of biomaterial-based nanoparticles in cancer immunotherapy has the potential to improve therapeutic efficacy while reducing unwanted side effects, making it a significant method and a new direction for cancer immunotherapy. Finally, the development of nanoparticle-based cancer vaccines is predicted to become a mainstream therapeutic capable of extending cancer patients' lives and increasing their quality of life. Recently developed approaches for using nanoparticles in cancer immunotherapy have enormous potential for improving cancer treatment. Cancer immunotherapy based on nanoparticles is anticipated not only to overcome the limitations of existing immunotherapy but also to generate synergistic effects via cooperation between nanoparticles and immune cells.

Keywords: Cancer immunotherapy, Tumor microenvironment (TME), Nanoparticle, Cancer antigens

Improvement of sugar in Stevia rebaudiana (Review)

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Introduction: Stevia rebaudiana is a shrub from Asteraceae family, it is native to South America. Its leaves produce a considerable amount of zero-calorie sugar, which is about 300 times sweeter than sucrose. Therefore, it can be used as a major source of natural sweetener. steviol glycosides are beneficial for people with obesity, diabetes and heart disease.

Methods: The ratio of rebaudioside A to stevioside determines sensory characteristics and flavor. S. rebaudiana have the bitter aftertaste. Various techniques have been used to reduce the bitter taste.

Results: In present study some strategies to improve the taste profile of steviol glycosides including The biotransformation of stevioside to rebaudioside A, specific extraction, microencapsulation, Interactions between steviol glycosides - Human receptors, and transformation was illustrated.

Conclusion: It seems that using a combination of two or several methods together can be useful. For example, the specific extraction method can be used in conjunction with the biotransformation of stevioside to rebaudioside A method. In any production process â€˜timeâ€™ and â€˜costâ€™ are two key factors which determine the economic production. Utilizing of each case, an economic evaluation must be performed.

Keywords: Stevia rebaudiana, steviol glycosides, bitter taste, stevioside, rebaudiosideA

Improving ethanol production in a commercial yeast strain by evolutionary engineering (Research Paper)

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Introduction: Saccharomyces cerevisiae is widely used for industrial production of ethanol. The tolerance to high ethanol concentrations, high-temperature is essential for process performance. To characterize ethanol-tolerant yeast strains, we performed adaptive laboratory evolution against higher concentrations of ethanol. Tolerance to ethanol is a key characteristic of the yeast Saccharomyces cerevisiae. Any increase in ethanol tolerance in the commercial strains led to faster and more complete fermentations, and may also allow the production of more alcohol. It appears that a large increase in ethanol tolerance requires complex changes in the yeastâ€™s genome. Several approaches that rely on the effect of (random) variation generated by evolutionary engineering or mutagenesis have successfully yielded strains with increased ethanol tolerance.

Methods: In the present study, to improve ethanol production the in the commercial â€œRaz170â€• strain, the parent strain was mutated physically and chemically. The mutants were screened using 1-butanol containing medium. The primary parent and the mutants were evolved within 144 days with evolutionary engineering strategy, while ethanol tolerance phenotype of selected strains was investigated.

Results: According to the increase in the maximum growth rate, 8 strains were selected including parental strain and mutants, and the amounts of ethanol production of these strains were evaluated after evolutionary adaptation tests. Ethanol production of R111 and R113 which were mutated with EMS and UV before the adaptive evolution test and then evolved at 9 and 11% v/v ethanol, respectively, was improved from 93.25 Â± 1.43 g/L to 102.25 Â± 2.13 and 99.5 Â± 0.93 g/L, respectively.

Conclusion: Evolutionary engineering, is a narrow-experimental evolution that mimics this natural phenomenon in laboratory towards the desired phenotypes that has been used excessively since two decades ago, and it has an extensive capabilities in creating capable strains in order to increase ethanol tolerance in industrial strains. To increase the genetic diversity of the primary population,

before starting the adaptive evolution experiments, mutation with ethyl methane sulfonate was used, which was more efficient than ultraviolet radiation in accelerating the evolution process to achieve the desired phenotype.

Keywords: Evolutionary engineering, Ethanol production, Mutation, Saccharomyces cerevisiae

In-silico analysis of Camelina sativa triacylglycerol pathway gene, CsPDCT1 (Research Paper)

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Introduction: Camelina sativa is an oil seed that can grow in a variety of climatic and soil conditions and requires less water, fertilizer, and pesticides than other oil seeds. It can be a new source for fuels and edible oils (Moser, 2010; Budin et al., 1995; Zubr, 1997). Camelina oil is rich in polyunsaturated fatty acids (PUFA) (approximately 50%) and contains linoleic acid (18: 2) and linolenic acid (18: 3 Ï‰3) in its oil composition (Eidhin et al., 2003). These unsaturated fatty acids are a source of unhealthy trans fats in the processing of many foods (Zimmermann et al. 2004; Dahlqvist et al., 2000; Cases et al., 2001). In oil seed cells, 18: 1 is unsaturated by 2 desaturase enzymes from the endoplasmic reticulum, FAD2 and FAD3, to 18: 2 and 18: 3 (Arondel et al., 1992; Okuley et al., 1994). Prior to unsaturation, 18: 1 must be added to phosphatidylcholine (PC), the only substrate known for the FAD2 and FAD3 desaturases (Stymne et al., 1978). Phosphatidylcholine: diacyl glycerol choline phosphotransferase enzyme (PDCT) is encoded by the ROD1 gene (At3g15820) in Arabidopsis and catalyzes transfer of the phosphocholine headgroup from PC to diacylglycerol, and mutation of rod1 reduces 18:2 and 18:3 accumulation in seed TAG by 40%. (Lu et al., 2009). In this study we have analyzed Camelina sativa genome to find homologues of AtROD1, which may have a crucial role on the component and quality of Camelina sativa oil and contribute to the control of poly unsaturated fatty acid synthesis in seeds.

Methods: A blast search was performed in the NCBI database using BLASTp to find protein sequences similar to AtROD1 (gene accession number At3g15820). Multiple sequence alignment of AtROD1 protein sequence and CsPDCT1 isoforms was performed using MUSLE program. The evolutionary analyses of selected sequences were conducted in MEGA7. Phylogenetic tree was generated on MEGA7 with maximum likelihood method. Using ROD1 Arabidopsis gene ID (At3g15820), information was obtained about the Camelina sativa PDCT1 gene expression from eFP (bar.utoronto.ca/efp_camelina/cgi-bin/efpWeb.cgi). The expression pattern of AtROD1 gene was investigated using microarray data available at Genevestigator (www.genevestigator.com). Conserved domains, regulatory elements, isoelectric points (Pi) and molecular weight (Mw) of PDCT1 were also evaluated

Results: By homology searches for protein sequences similar to Arabidopsis ROD1 at the NCBI database, three gene loci with relatively high homology to AtROD1 were identified on 3 different chromosomes of C. sativa. The first identified sequence with 86% amino acid similarity to AtROD1, called phosphatidylcholine-like diacyl phosphotransferase 1, is located on chromosome 19 of Camelina. This protein was abbreviated as CsPDCT1_1. The two other isoforms of this protein, CsPDCT1_2 and CsPDCT1_3 were

detected on chromosome 1 and 15 of Camelina respectively. Identification of three copies of the CsPDCT1 gene in C. sativa is consistent with the results of previous research on the Camelina plant. The C. sativa genome appears to be organized into three distinct versions (Hutcheon et al., 2010). PAP2_3 conserved domains of the PAP2 superfamily, the AtROD1 transmembrane conserved region and signal peptide are conserved domains found in CsPDCT1 sequences as well. Phylogenetic studies show a close relationship of ROD1 with phosphatidylcholine: ceramide choline phosphotransferases SMS1 and SMS2 from the LPT family in Homo sapiens. These enzymes catalyze the transfer of the phosphocoline head group from the phosphatidylcholine to the alcohol ceramide head group. SMS1 and SMS2 function as bidirectional lipid cholinephosphotransferases capable of converting phosphatidylcholine (PC) and ceramide to sphingomyelin (SM) and diacyl glycerol (DAG) and vice versa (Huitema et al., 2004). Analysis of the CsPDCT1 conserved domains indicates the existence of another domain of the PAP2 family called PAP2_C (Pfam profile PF14360) with a higher E-value (4.89e-03), which is located at the C terminal of the PAP2 domain. This domain is found in SMS and other proteins (Huitema et al., 2004). Phylogenetic tree analysis indicates a close relationship of three CsPDCT1 protein isoforms with their homologue in Capsella rubella. This analysis also shows that CsPDCT1 had a common ancestor with AtROD1 during a period of evolution. Using microarray data at the Genevestigator, the expression pattern of ROD1 gene at different developmental stages were evaluated. The ROD1 showed the highest expression at the stage of flowering and pod formation, and its expression decreased as the pods began to ripen. Data from the Arabidopsis gene expression atlas (Schmid et al., 2005) show that AtROD1 transcript levels are highest in seeds in which triacylglycerol accumulates. A search of the eFP site revealed that most of the changes in CsPDCT1 gene expression in Camelina are in the early to middle stages of seed development. Analysis of 1,500 bp upstream of PDCT1 genes at the PlantCare revealed that there are different cis regulatory elements in the promoter region of CsPDCT1 gene that can be classified in different groups such as stress, physiology, light and hormonal responses of the plant according to their role. Examination of gene expression under different conditions using microarray data in Genevestigator showed that ROD1 gene has the highest expression (4.5 fold) in the experiment of transferring etiolated Arabidopsis leaves from dark to light. Therefore, this gene seems to play an effective role in responding to light. The PDCT1L promoter of Arabidopsis plants (ROD1) and Camelina sativa have specific elements responsive to the abscisic acid and gibberellin. The promoter region of the Camelina CsPDCTB isoform has ABA-responsive ABRE elements. Water loss appears to induce ABA production, which in turn induces different genes (Shinozaki and Yamaguchi-Shinozaki, 2000). DRE and MBS were other drought responsive elements found in the promoter region of CsPDCT1. Interestingly, AtROD1 lacks MBS element. Drought response elements (DRE) are involved in various types of abiotic stress responses through ABA-dependent and non-ABA-dependent pathways. Microarray studies in Genevestigator also show a reaction of AtROD1 to ABA and a 3.63-fold decrease in its expression. Other elements include BOX-W1, HSE and TC-rich repeats and other elements that play a role in adjustment in stress and defense.

Conclusion: The study of Cis elements suggest the possible roles of CsPDCT1 proteins in biotic and abiotic stresses, especially drought stress. According to the regulatory elements in the promoter region of CsPDCT1L isoforms, these proteins seem to respond more effectively than its Arabidopsis homologue under drought stress. The existence of 3 copies of CsPDCT1 in C. sativa genome is an opportunity and a challenge for modifying oil content of this plant. Further studies are needed to determine the functional characteristics of CsPDCT1, .

Keywords: Camelina sativa, fatty acid, ROD1,, phosphatidylcholine diacylglycerol choline phosphotransferas

In-silico Analysis of suppressing of telomerase activity pathway by nc-RNA in human cancers (Research Paper)

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Introduction: Cancer is the leading cause of death worldwide and its prevalence is expected to increase dramatically as the world population grows . Telomerase holoenzyme has long been recognized as an important target in cancer therapy because most cancer cells depend on sustained and increased telomerase activity for sustained proliferation and longevity . This study aims to find critical genes in the telomerase pathway, inhibit oncogene, and amplify suppress gene by ncRNA.

Methods: In this study, at first, we using disgenet database for determining genes which are involve in telomerase pathway. Next, DAVID and Enrichr databases reveal critical genes from this gene list. For more analysis on our genes, we using GeneMANIA database. miRWalk, mirDB and TargetScan was used for determining miRNAs which potentially target these genes. Mir Path v.3 (Diana) was used to more analysis on our miRNAs. Sequence data were extracted from NCBI for antisense design and then design by IDTDNA.

Results: Our results confirmed that these genes of telomerase pathway activity had important roles in Melanoma, Thyroid cancer. Bladder cancer, Nasopharyngeal carcinoma, Basal cell carcinoma, Glioblastoma, Testicular germ cell cancer, Glioma, hepatocellular carcinoma, gastric cancer (TERT), Glioma, Glioblastoma, Basal cell carcinoma, carcinoma, basal cell, pancreatic cancer, breast cancer, colorectal cancer, hepatocellular carcinoma, gastric cancer, bladder cancer, (TP53), Nasopharyngeal carcinoma, Glioblastoma, Glioma, Melanoma, Basal cell carcinoma, pancreatic cancer, bladder cancer, bladder cancer (CDKN2A), Thyroid cancer, Bladder cancer, glioma, melanoma, hepatocellular carcinoma, gastric cancer (TERC). And these genes could be inhibited by hsa-miR-130b-3p for TERC (lncRNA), hsa-miR-491-5p for TERT, hsa-miR-1203 antisense for TP53 and CDKN2A. hsa-miR-1203 antisense: GGAGCCAGGATGCAGCTCAAGCCAC Hetro dimer with hsa-miR-1203: Maximum Î”G (kcal. mole-1): -184.1 kcal/mole

Conclusion: Telomerase is a holoenzyme complex and plays an important role in aging stem cells and immortal cancer cells. Scientific discoveries concerning the control of TERT and TERC and other proteins related to telomerase by microRNA have altered our knowledge of telomeres and telomerase biology.

However, some proteins in our study, such as PINX1, PML DKC1, WRAP53 have less evidence to relate to cancer but high potential for extensive research into cancer and treatment.

Keywords: microRNA, Telomerase , TERT, TERC, CANCER

Increased expression of glycolysis-associated genes including G6PD, STC2 and KIF20A with malignancy and poor prognosis in liver cancer patients (Research Paper)

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Introduction: According to the research, one of the hallmarks of cancer cells is metabolic alterations. The glycolysis pathway, rather than the oxidative phosphorylation pathway, can be used by cancer cells for energy. The purpose of this study was to explore the changes in the expression of glycolysis pathway genes and their relationship to the malignancies of liver cancer and the prognosis of patients.

Methods: Genes involved in the glycolysis process, which play a significant, role were discovered using a PubMed search. The alterations in the expression of potential genes relevant to the glycolysis pathway in liver cancer samples compared to normal were next analyzed using the OncoDB database, which contains transcript and clinical information produced by the cancer genome atlas. Changes in candidate gene expression were also assessed in relation to patient mortality rates. Furthermore, the association between the expression of glycolysis pathway candidate genes and clinical characteristics was evaluated.

Results: G6PD, STC2, and KIF20A genes discovered to be important in activating the glycolysis pathway in PubMed search results. The expression levels of these three genes increased significantly in liver cancer samples compared to normal and at least 2 times ($|logFC| > 1$, $P < 0.001$). According to the results of the expression analysis, increased expression of G6PD, STC2, and KIF20A has also been linked to a poor prognosis and a high death rate ($HR > 1$, $P < 0.01$). The connection between G6PD expression and clinical characteristics revealed that G6PD expression was considerably higher in stages 2 and 3 compared to stages 1 and 4 ($P < 0.01$). STC2 was not linked to stage specificity, although KIF20A expression was considerably higher in stages 2 and 3 than in the other stages ($P < 0.01$).

Conclusion: Our findings revealed that the expression levels of genes implicated in the glycolysis pathway, such as G6PD, STC2, and KIF20A, increased significantly in cancer samples compared with controls, and this increased expression was related to a higher death rate. Their expression was significantly associated with the higher stages, according to the findings. Our results indicate that glycolysis pathway genes could be valuable therapeutic and diagnostic options, and that inhibiting the glycolysis process could aid patients.

Keywords: glycolysis pathway, G6PD, STC2, KIF20A, liver cancer

Induced Pluripotent stem cell therapy for Multiple sclerosis : a mini review (Review)

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Introduction: Multiple sclerosis (MS) is a neurodegenerative autoimmune disease that involves young adult people. Although a large spectrum of cell therapeutic approaches for MS has been unsuccessful, some of them are useful in focal myelin disease .Induced pluripotent stem cell (IPSC) therapy is one of kinds of autologous cell transplantation therapy. First time embryonic cell of mouse and human fibroblast cell were used to generate IPSCs.

Methods: IPSCs are somatic cells in adult individuals which can be reprogrammed by some particular factors . Moreover IPSCs have potency to convert into neural precursor cells (NPCs) and oligodendrocyte precursor cells (OPCs)

Results: In several studies mouse IPSC-NPCs (mi IPSC-NPCs) reduced the amount of damage tissue and demyelination areas and clinical score the experimental autoimmune encephalomyelitis (EAE) .

Conclusion: Furthermore, mi IPSC-NPCs have efficacy to protect the differentiation and survival amount of oligodendrocytes and limit the transcriptional changes related to clinical score of EAE by secreting leukemia inhibitory factor (LIF). They can decrease the blood brain barrier (BBB) damages as well as, reduce the infiltration of T cells into the neural tissue.

Keywords: Experimental autoimmune encephalomyelitis Â· Induced pluripotent stem cell .Multiple sclerosis.

Induction of thermal pain and inflammation in the foot injection of capsaicin compared with formalin in male rats (Research Paper)

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Introduction: Stimulation of peripheral pain receptors by chemical and inflammatory agents leads to pain. Injection of formalin as a model of chemical pain causes pain in two stages: neurogenic (direct stimulation of receptors) and inflammatory (due to release of inflammatory agents). Red pepper capsaicin also directly stimulates peripheral pain receptors but may not induce inflammatory pain processes. This study compares the effect of foot injections of different concentrations of capsaicin with formalin.

Methods: 200 to 250 g male Wistar rats (n = 7) were used. Foot injections of 0.5% formalin and also in three groups of concentrations of 0.20 mg/ lit, 0.10and 0.5capsaicin were performed to induce inflammatory pain and inflammation and changes in pain sensation were recorded within one hour after injection.

Results: The use of capsaicin solution in a dose-dependent manner reduced the amount of thermal pain at a concentration of 20 mg/lit(P <0.01 **), a concentration of 10 mg/lit (P <0.05 *) but a significant difference at a concentration of 5 mg/lit compared to before injection It did not cause it. Also, only at a concentration of 20 mg/lit we see significant inflammation compared to before the injection (P <0.05 *), which is significantly less than the inflammation caused by formalin (P <0.01 **).

Conclusion: :Recent research has shown that capsaicin exerts its analgesic (thermal) effect by removing substance P in pain-related sensory fibers by first attaching to the pain receptor and activating this channel.(Painful effect) but then the removal of substance P makes sensory neurons insensitive and analgesic.

Keywords: Thermal pain, inflammation, rat,Capsaicin

Integrated system biology investigation (in-silico) of Co-expression of the lncRNAs and mRNAs associated with the immune system in Lupus (SLE) (Research Paper)

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Introduction: Systemic lupus erythematosus (SLE) is a prototypical autoimmune disease, characterized by overactive inflammation and aberrant activation of lymphocytes. (1) miRNAs, discovered non-coding RNAs, regulate gene expression at the post-transcriptional level by base pairing with 3â€™UTR of their targeted mRNAs annotated as to their targetome. Moreover, C-X-C motif chemokine 10 (CXCL10) was significantly elevated in a systemic lupus erythematosus (SLE) cohort compared to healthy donors. STAT1, CCL2, and CXCL10 are potentially useful indicators of therapeutic action in SLE patients. CXCL10 was correlated with type-I IFN in high STAT1 patients similar to that in untreated patients. (2) Analyzing the expression mRNAs microarray from childhood-onset lupus (cSLE) skin lesion tissues and normal skin with GSE148810. (3)

Methods: miRNAs were regained from miRwalk and Enrichr databases, followed by examining their expression in childhood-onset lupus (cSLE) skin lesion tissues using GEO and DAVID database. Interaction lncRNAs and mRNAs by Enrichr databases and lncHUB databases. The miRWalk was used to analyze miRNAâ€“mRNA interactions. The Pathway enrichment analysis was carried out using the online databases KEGG and Reactome. The expression of lncRNAs in different tissues has been examined by the lnCAR databases. comparing the expression of genes in different tissue by Gepia2 databases and The protein-protein interaction analysis by STRING online software.

Results: We found that CXCL10, CXCL11, CXCL9, and IRF1 mRNAs had the most significant expression changes (adj.P.Val<0.05). We have examined interactions between lncRNAs and mRNAs. The expression of mRNAs including CXCL10 and CXCL9 have miR-1278 and CXCL9 and CXCL11 have miR-379. Furthermore, CXCL9, CXCL10, and CXCL11 have similar microRNAs including mmu-miR-590-5p and mmu-miR-21. We found LncRNAs including Linc02195, PSMB8-AS1, and Linc02446 that are common in CXCL9, CXCL10, CXCL11, and IRF1. The existence of CXCL9, CXCL10, CXCL11, and IRF1 had CeRNA with lncRNAs, which indicates the existence of a complex network that can be used in gene therapy or drug. Also, we have a high expression of PSMB8-AS1 in gastric cancer. Also, we have a high expression of PSMB8-AS1 in gastric cancer. There are common pathways between CXCL9, CXCL10, and CXCL11 including Toll-like receptor signaling, Cytokine-cytokine receptor interaction, and chemokine signaling pathway. Additionally, CXCL10 is involved in TNF signaling pathway. The TNF signaling pathway

plays an important role in various physiological and pathological processes, including cell proliferation, differentiation, apoptosis, modulation of immune responses, and induction of inflammation. CXCL10 is a potentially useful indicator of therapeutic action in SLE patients.

Conclusion: We identified several hub lncRNA-mRNA networks involved in regulating various biological processes in systemic lupus erythematosus (SLE). CXCL9, CXCL10, CXCL11, IRF1, and also, Co-Expression LINC0219, LINC02446, PSMB8_AS1 could be prognostic biomarkers in the Immune system. Moreover, LINC0219, LINC02446, PSMB8_AS1 play a role in the Cytokine-cytokine receptor interaction pathway.

Keywords: cSLE, IRF1, CXCL10, PSMB8-AS1, Network complex, TNF signaling pathway

Investigate the relation between GPR45 gene and lncRNA-CYTOR in anaplastic astrocytoma (Research Paper)

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Introduction: Anaplastic astrocytoma (AA) is a rare, malignant brain tumor that arises from astrocytes, the supportive cells in the nervous system. anaplastic astrocytomas (grade III) may also be called a â€œgrade III gliomaâ€• or â€œhigh-grade glioma.â€• Symptoms of anaplastic astrocytoma can result from an increase of pressure in the brain. This occurs as the tumor grows larger and takes up space, compressing healthy brain tissue within the fixed volume of the skull. If not diagnosed early, tumors can grow large enough to block the normal flow of cerebrospinal fluid in the brain. In this study, the regulation of GPR45 gene and the effect of lncRNA-CYTOR on it in anaplastic astrocytoma were examined using bioinformatics databases.

Methods: First, this gene was structurally analyzed in GeneCards then GPR45-related single nucleotide polymorphisms (SNPs) and microRNAs were found in GWAS Catalog and NCBI databases. Ultimately, the LncRNADisease database (version 2.0) helped to find a long non-coding RNA (lncRNA) connected with the GPR45 gene signaling pathways.

Results: The GPR45 gene, which encodes a member of the G protein-coupled receptor (GPCR) family and is located on chromosomal position 2q12.1, mediate signaling processes to the interior of the cell via activation of heterotrimeric G proteins. According to findings from the GEPIA2 database, the GPR45 gene is highly expressed in astrocytoma. The analysis Indicated that the incidence of the SNP:rs2576789 can lead the cells to Anaplastic astrocytoma and outcome the involved miRNA-4435-1 and lncRNA-CYTOR in this process. Through the process of this disease, the disease-associated SNP is located on the mRNA and the miRNA-4435-1 binds to 3â€™UTR of GPR45 mRNA as an activator. When lncRNA-CYTOR, binds to miRNA-4435-1, turns on miRNA-4435-1 and the GPR45 gene is activated, finally intensifies the tumorigenesis of anaplastic astrocytoma.

Conclusion: The present study inferred that, the interaction of lnc-CYTOR with rs2576789 could be useful biomarkers for the diagnosis of anaplastic astrocytoma. The miRNA-4435-1 proves also that GPR45 is an effective gene in anaplastic astrocytoma outbreak and its tumorigenesis, so there is hope for early diagnosis this malignant brain tumor.

Keywords: Anaplastic astrocytoma, miRNA-4435-1, rs2576789, lnc-CYTOR, GPR45

Investigating the Effect of Thiosemicarbazones complexes Cu on Expression Changes of LncRNA TUG1 in Acute Lymphoblastic Leukemia (Research Paper)

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Introduction: Acute lymphoblastic leukemia (ALL) is a kind of leukemia that affects lymphoid progenitor cells in the bone marrow, blood, and extramedullary locations. While 80 percent of ALL cases occur in children, it is a life-threatening condition in adults. ALL has a bimodal incidence pattern, with the first peak occurring in childhood and the second peak happening around the age of 50. While dose-intensification techniques have improved results for pediatric patients, the prognosis for the elderly is still quite bad. Despite a high percentage of induction chemotherapy response, approximately 30â€“40% of adult ALL patients will achieve long-term remission. TUG1 appears to play a role in tumor growth and cell metabolism through regulating cell proliferation, invasion, metastasis, apoptosis, differentiation, and treatment resistance, according to several studies. Thiosemicarbazones are effective against a variety of tumors, including leukemia, pancreatic cancer, breast cancer, non-small cell lung cancer, cervical cancer, prostate cancer, and bladder cancer. The goal of this study was to see how the Cu-thiosemicarbazones complexes affected the expression of LncRNA TUG1 in the Jurkat E6.1 cell line.

Methods: In this research, appropriate doses of the thiosemicarbazones complexes Cu were prepared according to the IC50 of the drug that consists of 15 and 16 ÂµM. The Jurkat E6.1 cell line was treated by Cu at 72 hours after cell passage. The expression changes of LncRNA TUG1 and GAPDH as the housekeeping gene were investigated using Real-Time PCR after RNA extraction and cDNA synthesis. Finally, Rest 2002 Software was used to analyze the data, and Excel was used to create diagrams.

Results: The Results of the research showed that after 72 hours of treatment with thiosemicarbazones complexes Cu at 15 and 16ÂµM concentrations, the expression of LncRNA TUG1decreased significantly as compared to the control group. According to the findings, doses of 15 and 16ÂµM of Cu over 72 hours were the optimal concentrations and time for this drug's effect. The expressions

of LncRNA TUG1 were 1.968 and 2.369 at the specified concentrations and times.

Conclusion: According to the findings of the study of expression changes in LncRNA TUG1 as a Tumor suppressor gene after treatment with thiosemicarbazones complexes Cu, both concentrations of the drug successfully increased LncRNA TUG1 expression. Overall, thiosemicarbazones complexes Cu had a positive effect on the LncRNA TUG1 increased mechanism over 72hour, and this increase in expressions was statistically significant (p-value 0.001). According to evidence, Cu-thiosemicarbazone complexes have a high anticancer potential and affirmative treatment of that.

Keywords: Thiosemicarbazones complexes Cu, cDNA, GAPDH, LncRNA TUG1

Investigating the market of derivatives tropane alkaloids and the trade of processed products (Review)

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Introduction: The present study is a review that was collected according to the research of researchers in production and trade of medicinal and aromatic planes specially the derivatives tropane alkaloids. Medicinal and aromatic plants (MAPs) have been used for various purposes in many fields from medicine to cosmetics for thousands of years (Yildirim, 2021). In recent years, with the increasing awareness of sustainable development, environmental protection and healthy life, the production and trade of medicinal and aromatic plants has also increased. Today it is estimated that there are 422,000 plant species in the world and 50,000 of them are medicinal and aromatic plants (Shikov et al., 2021). The current global trade in medicinal plants is more than 150 $ billion, which is projected to expand to more than 450 $ billion by 2025 and by 2050 (Euromonitor, 2020). Tropane alkaloids are an important class of secondary metabolites that occur mainly in many members of the plant family Solanaceae. The Atropine, hyoscyamine and scopolamine are found in a variety of solanaceous plants including Atropa belladonna and Datura stramonium (Huang et al., 2019). Their biosynthesis occurs in the plant roots, which provides the advantage to study the biosynthesis using the plant hairy roots culture (Huang et al., 2019). Also, Most of the new tropane alkaloids were discovered in the family Solanaceae (Afewerki et al., 2019).

Methods: However, for the following purposes, we reviewed new articles and reputable sites; 1- Investigating the market of derivatives tropane alkaloids and the trade of processed products in the world specially in Iran 2- Possibility of producing derivatives tropane alkaloids from plant resources and if possible, their commercialization

Results: The results of our research show that important companies such as Sigma-Aldrich, Pharmafair, Meridian (USA), Winzer, (Denmark), Cjauvin, (France, Suisse), Stella, (Belgium, Luxembourg), Novartis, Delvin Formulations, Inga Laboratories and German Remedies Private (India) have a decisive role in the production and sale of derivatives tropane alkaloids. Capharma is the world leading manufacturer in global Atropine market with the market share of 9.19%, in terms of revenue, followed by Resonance Laboratories, Rolabo Outsourcing, Minsheng and CR Double-Crane. The

global Atropine market is valued at 530.2 million USD in 2020 is expected to reach 469.6 million USD by the end of 2026. The average price of Atropine (5 ml) for current year was 60 $, Hyoscyamine (0/125 mg) was 20 $ and Hyosyne (0/125 mg) was 17 $. However, we did not obtain information and data about the production of derivatives tropane alkaloids in Iran, and there is a proper opportunity for us to produce these compounds by using the potentials of medicinal plants in Iran and by using the capabilities of plant breeding science, biotechnology and phytochemistry. Finally, we can help the country's economy by producing and exporting these products.

Conclusion: In conclusion, we can claim there is a proper opportunity for us to produce these compounds by using the potentials of medicinal plants in Iran and by using the capabilities of plant breeding science, biotechnology and phytochemistry. Finally, we can help the country's economy by producing and exporting these products.

Keywords: medicinal plants, derivatives tropane alkaloids, commercialization, Datura stramonium

Investigating the role of hsa-miR-1256-5p as therapeutic targets involved in PI3K-Akt-mTOR pathway in coronary heart disease (Research Paper)

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Introduction: Coronary heart disease (CHD), which is known as coronary artery disease (CAD), is caused by the buildup of plaque in the arteries that supply oxygen-rich blood to the heart which is one of the main causes of hospitalization worldwide and has high morbidity. NcrRNAs (miRNAs) play an important role in the pathogenesis of cardiovascular diseases that can regulate protein translation by either complete or incomplete pairing with the target gene, or by inhibiting expression of downstream target proteins. MiRNAs have emerged as a novel class of gene regulatory elements with conserved roles in development and disease .So this study purposes to evaluate the association between hsa-miR-1256-5p and PI3K-Akt-mTOR pathway.

Methods: Specifications of miRNAs were obtained through mirbase, HMDD and miRdSNP. To identifying target genes, miRTarBase, MIRWALK2.0, TargetScan, DIANA Tools were used. Venn diagram used to identify common target genes between MiRNAs. The signaling pathways for target genes which had high expression difference were observed from the DAVID database and the pathways associated with CHD were stored for interpretation. The network of genes was obtained from GENE MANIA.

Results: The result demonstrated the expression levels of related proteins in the PI3K-Akt-mTOR pathway in which hsa-miR-1256 -5p prevents cell growth and proliferation by activating PETEN which blocks AKT. In other side of the pathway mentioned microRNAs inhibit MTOR by blocking PI3KACT and AKT and effect on adhesion increasing by preventing cell survival and proliferation by blocking BRAF and RAS which active MEK1/2, ERK1/2 , RAF and BCL2 through phosphorylation.

Conclusion: In this study we found that the role of hsa-miR-1256-5p in CHD is associated with the PI3K-Akt-mTOR pathway in whic hsa-miR-1256-5P might be a novel bio-marker for coronary heart disease. PI3K/Akt pathway is involved in the occurrence and development of vascular physiology and pathology which plays a vital role in the occurrence and development of CHD. Activating the PI3K/Akt signaling pathway can reduce reactive oxygen species (ROS) and lipid deposition levels, inhibit plaque formation, and reverse the progression of CHD.

Keywords: Coronary heart disease, Signaling pathways, MicroRNA, target genes

Investigating The Role of hsa-miR-147 as Therapeutic target in JAK/STAT pathway In Hypertension (Research Paper)

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Introduction: Hypertension is a major public health problem among the elderly population worldwide that is related to increasing risk of adverse cardiovascular events which is a major risk factor for the development of stroke, coronary artery disease, heart failure, and chronic renal failure. Diagnosis and treatment progression have key role in exploration of biomarkers for hypertension. MicroRNAs are small non-coding RNAs that regulate post-transcriptional gene expressions. They have been shown to play an important role in fibrogenic process in multiple organs.so this study aims to investigate the relationship between hypertension and microRNAs in JAK/STAT pathway.

Methods: By using mirbase, HMDD and miRdSNP, miRNA properties were obtained. The miRTarBase, MIRWALK2.0 and TargetScan, target genes were identified. Venn diagram used to identify common target genes between MiRNAs. Using DAVID and KEGG, signal paths were obtained and the pathways associated with diabetes were interpreted. The gene network was obtained through GENE MANIA.

Results: We identified hsa-miR-23a-5p as the best miRNA, its target genome and associated cell signaling pathways. Then, the findings presented that binding of the cytokine (IL-6 or IL-11) to its unique receptor (IL-6R or IL-11R) triggers the homo dimerization of GP130. This results that hsa-miR-147 phosphorylates JAK1, JAK2, and Tyk2, which phosphorylate intracellular tyrosine residues that serve as docking sites for STAT3 in hypertension .ET1 and Ang II exert their action through the activation of receptors that belong to a large family of transmembrane guanine nucleotide-binding protein-coupled receptors (GPCRs). JAK and STAT are constitutively expressed by hsa-miR-147 and directly coupled to this receptor. The binding of ETI/Ang II which is activated by hsa-miR-147, induces the phosphorylation of tyrosine in the JAK2 kinases, which in turn activates STAT1 and STAT3. In addition, hsa-miR-147 can stimulate the activity of PKC Î´ by activating ET-1, which phosphorylates STAT3.

Conclusion: : Hypertension is a disease that affects the pulmonary vasculature, increasing pulmonary vascular resistance and pulmonary pressure, which leads to compensatory right ventricular hypertrophy that can turn into right ventricular failure. The JAK/STAT pathway is crucial in transmitting signals from many cytokines and growth factors into the nucleus regulating gene expression and functions. In this study we found that the role of hsa-miR-147 in hypertension is associated with the JAK/STAT pathway in

which hsa-miR-147 might be a novel bio-marker for hypertension. The potential role of miR-21 as a new target for predicting and treating hypertension is also explored.

Keywords: Hypertension, JAK/STAT pathway, MicroRNA, Target genes

Investigating the role of ncRNAs as therapeutic targets involved in ERK | MAPK pathways through Major depressive disorder (Research Paper)

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Introduction: Major depressive disorder is one of the most common neuropsychiatric diseases. Epigenetic mechanisms can play a role in increasing depression risk following adverse life events that provide a mechanism for integrating genetics and environmental factors. Epigenetics refers to processes that affect gene expression and translation in which DNA sequence changes are not involved while it includes methylation of DNA (mDNA), microRNAs (miRNAs), and long non-coding RNAs (lncRNAs). Recently, miRNAs and lncRNAs have emerged as a novel class of gene regulatory elements with conserved roles in development and disease. Thus, the purpose of our study was to investigate the interaction between microRNAs, lncRNAs, and gene expression in the pathway.

Methods: The feature of microRNA was achieved from miRBase, human disease database (HMDD), and miRdSNP databases. Target genes were identified by investigation in miRTarBase and miRWalk databases. Venn diagram was used to identify the shared target genes between miRNAs. The GSE54562 derived from the Gene Expression Omnibus (GEO) datasets was analyzed to obtain potential therapeutic targets of MDD. The differentially expressed genes (DEG) between MDD and normal tissue from human brain anterior cingulate cortex were obtained using GEO2R. The gene ontology function and path enrichment analysis were performed from Kyoto Encyclopedia of Genes and Genomes (KEGG) to identify pathways and annotation functions of DEGs. LncRNAs associated with overexpressed genes were found through LncRRIsearch and their relationship with depressive disorder was investigated by LncRNADisease 2.0. The GeneMANIA database was used to map the relationship between genes in the form of a gene network.

Results: Through the bioinformatics challenges in the current study, the hsa-miR-22-5p, hsa-miR-155-5p were found as the best miRNAs, their target genome and associated cell-signaling pathways. The findings presented that this miRNAs had a key role in both â€œERKâ€□ and â€œMAPKâ€□ signaling pathways. . The result demonstrated that hsa-miR-22-5p, hsa-miR-155-5p inhibit Ras by blocking Raf-1, MEK1/2 which active ERK and c-fos through

phosphorylation in MAPK pathways. These microRNAs inhibits (IL1b-IL6-IL15-lif-tnf) by blocking MKK4/7, JUNK1/2 in TNF pathway in MDD patients.

Conclusion: Increasing proof supports a critical role of mitogen-activated protein kinases (MAPKs), specially the extracellular signal-regulated kinase (ERK) subclass MAPK, in pathogenesis, symptomatology, and treatment of MDD in which ERK signaling was significantly downregulated in the prefrontal cortex and hippocampus, middle regions implicated in depression. Expression of phosphatases (MKP-1, MKP-2, PP1) improved in the prefrontal cortex and hippocampus of depressed human or animals. Intracranial injection of the MKP-1 inhibitor reversed the decreased hippocampal ERK phosphorylation and decreased behavioral responses to stress. The lncRNAs can be diagnostic biomarkers for MDD, we aimed to quantify the levels of DISC1 and DISC2 lncRNA transcripts. These facts verified that DISC1 and DISC2 lncRNA expression relates to an improved danger of MDD and can contain numerous molecular mechanisms. Our study discovered that the transcript stages of DISC1 and DISC2 lncRNA can be taken into consideration as a great putative biomarker for patients with MDD.

Keywords: Depression disease, MAPK, MicroRNA, ERK, LncRNA

Investigation Ashwagandha on human breast cancer cell line by Meta analysis vision (Research Paper)

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Introduction: Cancer treatment with herbal compounds is an option with the minimum side effects. Ashwagandha as a plant is useful for reducing stress, boosting immune system, and it contains Withaferin A, as an inhibitor of angiogenesis. In this study, we showed biological pathways changes in MCF-7 cells after treating by Ashwagandha.

Methods: The GSE144235 dataset in NCBI was analyzed with GEO2R, the control group (MCF-7, DMSO) and the test group (MCF-7, Ashwagandha _125mcg/ml) have been considered with p.value less than 0.05 ;then to know biological pathways, gene ontology was performed using DAVID database for the list of genes with logFC greater than 0.6 and also less than -0.6.

Results: The results clearly show the difference in the expression of genes between the control and test groups. Genes like CCNB1,CDK4,CDC20 involved in cell division and also genes like CDK1,EGFR2, TP53involved in apoptotic process had less expression in test group comparing to the control group.

Conclusion: The gene expression changes in biological pathways like apoptosis and cell division after treating MCF-7 by Ashwagandha shows that it can be effective on breast cancer because some up-regulated genes in cancer decreased their expression after treatment by Ashwagandha. This condition indicates that the expression of test group was close to normal situation and this plant is useful to make medicine for breast cancer.

Keywords: Breast cancer; Biological pathways; Ashwagandha; Apoptotic process.

Investigation of a long non-coding RNA through ASD, Breast cancer and prostate cancer (Review)

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Introduction: Abstract: Background. The retinoblastoma (RB1 or RB) is a tumor suppressor gene which is located on Chromosome 13q.14,2. The Neurobeachin (NBEA) gene is an important factor in Autism Spectrum Disorder (ASD). Phosphatase and tensin homolog (PTEN) is a tumor suppressor gene which is located on Chromosome 10q23,3 and its inactivation is a frequent event in many cancers such as breast and prostate cancers. PTEN is also involved in ASD. P53, PTEN and RB1 are tumor suppressor genes, which are frequently mutated in breast cancer, but new researches have shown that at least one of these three genes must be inactivated for oncogenesis. The co-loss of BRCA2-RB1 can enhance the progress of prostate cancer even in primary phases and drive it to more aggressive one and a possibility of FFL (feed-forward loop) between BRCA2 and RB1 expression in prostate cancer. MicroRNAs (miRNAs) are non-coding RNAs which regulate gene expression. Some of miRNAs are associated with oncogenesis, metastasis and tumor suppressing roles in normal cells that are called oncogenic miRNAs or oncomirs. The aim of this study was finding more related links between our knowledge based on previous researches through bioinformatics databases.

Methods: Materials and Methods. General information about RB1, BRCA2, PTEN, NBEA, and their interactions were acquired by previous studies. The miRWalk database was used to find the miRNAs associated with desired genes. The lncRNASNP2 database was applied to achieve the involved long non-coding (lnc) RNAs involved in ASD, breast and prostate cancers. The miRBase database and TAM (Tool for Annotations of Micro RNAs) helped to find more details about miRNAs such as sequencing, annotations, structures, and their related diseases.

Results: Results. The bioinformatics predictions showed that has-miR-6870-5p is a common miRNA between RB1 and BRCA2, PTEN, and NBEA genes. The lnc:NONHSAT190283.1 is involved in breast neoplasia, prostrate neoplasia and ASD. The miRBase database predictions revealed that has-miR-21-5p and has-miR-6870-5p can regulate each other. The miRWalk database showed that has-miR-6870-5p is a shared miRNA for RB1, BRCA2, PTEN, and NBEA genes and it can regulate their expression in a same way. The bioinformatics predictions showed the lnc: NONHSAT190283.1 as a common regulator between has-miR-21-5p and has-mir-6870-5p. The data showed

Autism Spectrum Disorder, breast and prostate cancers that are linked to lnc: NONHSAT190283.1, has-miR-21-5p and has-miR-6870-5p.

Conclusion: Conclusion: According to our bioinformatics data, the common NONHSAT190283.1 between has-miR-21-5p and has-mir-6870-5p, it is possible that there would be a connection between RB1, BRCA2, PTEN and NBEA genes might be used as biomarkers through diagnosis of studied disorders.

Keywords: Keywords: Autism, cancer, has-miR-21-5p, has-miR-6870-5p, NONHSAT190283.1

Investigation of inhibitory effect of novel synthetic 1,3,4-thiadiazole derivatives on acetylcholinesterase enzyme. (Research Paper)

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Introduction: Alzheimerâ€™s disease (AD) that is the most common cause of dementia is a progressive neurodegenerative disease which ultimately leads to death. According to the cholinergic hypothesis of AD pathogenesis, the clinical features of AD are attributed to the decrease of acetylcholine, a neurotransmitter participating in memory and learning process, in the brain hippocampus and cortex [3,4]. Therefore, the administration of acetylcholinesterase enzyme (AChE) inhibitors is very common for the symptomatic treatment of mild to moderately severe forms of AD. AChE inhibitors are also utilized to manage the other forms of dementia and CNS disorders such as Parkinsonâ€™s disease (PD), dementia with Lewy bodies, Downâ€™s syndrome, and Korsakoff disease. Nowadays, worldwide research is being conducted to design and develop novel potent AD drugs with higher therapeutic efficacy and less side effects. Thiadiazole is a common and important heterocyclic compound containing two carbon atoms, two nitrogen atoms and a sulfur atom. There are several thiadiazole isomers, of which 1, 3,4-thiadiazole has been studied the most. 1, 3,4-thiadiazole derivatives exhibit a wide range of biological activities such as antimicrobial, antifungal, antioxidant, anti-inflammatory and anticancer. In this paper, the effect of eight novel synthetic compounds containing 1,3,4-thiadiazole ring on the inhibition of AChE activity has been investigated.

Methods: Ellman method was used to evaluate the ability of the novel synthetic thiadiazole derivatives to inhibit AChE (from electric eel) and the results were reported as the half maximal inhibitory concentration (IC50) of the derivatives. To determine the IC50 of the thiadiazole compounds, the enzyme activity were determined in the absence and presence of at least seven different concentrations of the derivatives. Each concentration was analyzed in triplicate and neostigmine was used as the reference compound. All the enzyme assays were performed in 96-well plate with final volume of 200 Âµl. The assay mixture contained 0.1 M potassium phosphate buffer (pH 8.0) and the enzyme (AChE) and Ellmanâ€™ reagent (DTNB) with the final concentrations of 0.1 unit/ml and

0.5 mM, respectively. The compounds were incubated with the assay mixture at 25 oC for 10 minutes. The substrate (acetylthiocholine iodide) was then added to the assay with final concentration of 1 mM and the absorbance was read after 10 minutes at 405 nm by a microplate reader. A sample containing all the assay components except the enzyme was applied as blank. Finally, the percentage of enzyme inhibition at each concentration of the compounds was calculated and IC50 values were determined using the dose response curves plotting the inhibition percentage versus the logarithm of inhibitors concentration. The results were reported as the mean Â± standard deviation (SD).

Results: All the eight thiadiazole derivatives studied were capable of inhibiting AChE. The IC50 values of the compounds were variable between 0.016 Â± 0.0015 and 0.084 Â± 0.003 ÂµM. The IC50 value of the most active compound, 4d, was almost equal to that of the reference compound (0.014 Â± 0.0015).

Conclusion: In this study, the anticholinesterase activity of eight novel synthetized compounds containing 1,3,4-thiadiazole ring was studied. The results showed that the compound 4d is the powerful inhibitor of AChE and has a great potential for further studies.

Keywords: Alzheimerâ€™s disease (AD), Acetylcholinesterase enzyme (AChE),1,3,4-Thiadiazole, Ellman method.

Investigation of microRNAs associated with the sickle cell disease (Review)

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Introduction: Sickle cell is one of the most common genetic and hematological disorders in the world. This disease gradually causes problems for brain, kidneys, bones, vascular system and lungs. Recent studies have indicated that accelerating the detection and investigation of disease interveners may change the pathway of disease.

Methods: The analysis on expression of genes involved in sickle cell disease was examined on GSE11524 through the GEO2R package in the GEO dataset. The most differentially expressed genes were analyzed in DAVID database in order to identify the most effective gene in incidence of sickle cell disease. Additionally, the microRNAs associated with this gene were identified using miRWalk database. The Human microRNA Disease Database (HMDD) helped to identify the microRNAs affecting the sickle cell disease.

Results: The analyses showed that the most effective gene in sickle cell disease is hemoglobin subunit beta (HBB) gene. Regarding the fact in the miRWalk database, hsa-mir-34a-5p and hsa-mir-34a-3p were identified as HBB-related microRNAs. Furthermore, by using of HMDD database it was found that has-mir-34a is a potential microRNA in the process of sickle cell disorder through downregulation of gene, which caused by miRNA.

Conclusion: Knowing the factors influencing the expression of the target gene may be able to change the pathway of the disease and recognizing the involved microRNAs as markers may help us to control diseases. More studies that are detailed are needed to be done on the role of microRNAs related to HBB gene.

Keywords: Genetic disorder, non-coding RNA, Bioinformatics, Databases

Investigation of the functional relationship of MicroRNA with its related factors in cardiovascular disease: from cancer to cardiovascular (Review)

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Introduction: Coronary artery disease (CHD) is a complex disease, a major threat to human health, and the leading cause of sudden cardiac death in adults worldwide. CHD occurs as an environmental and genetic factor. Only known environmental and genetic effects can explain a small part of the variability in CHD risk, which is a major barrier to its prevention and treatment, so the need for effective prevention strategies is essential. MicRNAs are also non-coding RNA molecules that act as regulators of post-genre expression Transcriptions turn off genes.MicRNAs in cardiovascular disease (CHD) have been studied as promising biomarkers for disease diagnosis, prognosis, and monitoring. Physiology, pathology, cardiac hypertrophy, and tone maintenance and response to vascular injury. MicRNAs individually as well as in a complex regulatory network affect heart growth and homeostasis. MicRNAs are identified in patients with coronary artery disease and atherosclerosis. However, their association with risk factors Cardiovascular, including hyperlipidemia, hypertension, obesity, diabetes, inactivity, and smoking is unclear. This study investigates the role of microRNAs and their interaction with environmental factors in CHD and aims to investigate the role of MicRNAs as markers. New bio-potential for cardiovascular disease.

Methods: This secondary study with the Narrative Review approach, in 2022 by searching for keywords such as MicroRNA, Neoplasm, Primary MicroRNA, Hypertrophies, Biology Markers, Coronary Heart Disease and Atherosclerosis in the MESH database as well as valid databases between Internationally, PubMed, Science Direct, Web of Science and Scopus. This study was finally reviewed by extracting 15 articles, of which 10 articles were included in the study

Results: Based on studies from various studies, the results are that multiple microRNAs (miRs) are small RNAs that target multiple pathways. High and regular daily exercise significantly reduced the risk of CHD. The data showed that a light diet was significantly associated with a reduced risk of CHD, while a family history of CHD, anxiety, and alcohol consumption was significantly associated with an increased risk of CHD. Two types of MicRNA (miR-126) And miR-148) in combination with several risk factors could have played a common role in the development of CHD. Therefore, it is necessary to manage patients with CHD in all directions and on multiple levels. CHD was associated with

changes in MicRNA expression profiles as well as risk factors, such as abnormal lipid metabolism. Thus, miRNAs may be potential biomarkers of CHD. However, there are limitations to the use of MicRNAs. These include costs and several confounding factors that may affect the MicRNA profile.

Conclusion: According to the results, a better understanding of the key processes that lead to pathophysiological changes that underlie the disease is of great importance. Many miRNAs are also expressed in the fetal heart after birth and in adults. Their abnormal expression or genetic deletion is associated with abnormal differentiation of heart cells, impaired heart growth, and impaired heart function. A considerable body of evidence suggests that miRNAs are involved in the development of CVD and suggest them as attractive diagnostic biomarkers and therapeutic tools.

Keywords: MicroRNA, Neoplasm, Primary MicroRNA, Hypertrophies, Biology Markers, Coronary Heart Disease and Ath

Isolation and identification of two yeast strains from Iranian dairy sources as a potential safe microbial novel food. (Research Paper)

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Introduction: Nowadays, microbial biotechnology is receiving worldwide attention by introducing alternative food sources which are necessary to achieve sustainable food and feed security. Yarrowia lipolytica is a non-pathogenic generally regarded as safe yeast (GRAS) for industrial productions by the American Food and Drug Administration. Yarrowia lipolytica biomass, which is classified in the category â€˜Food consisting of, isolated or produced from microorganisms, fungi or algaeâ€™ is considered as a novel food and a novel food ingredient and it can be a component of food supplements and a component of selected foods in the form of yeast cells, dried and deprived of metabolic activity. One of the most important obstacles to the industrialization of the Y. lipolytica platform is the lack of naturally versatile strains to make the platform more robust for increased yield and productivity.

Methods: in the present study, we attempt to isolate and characterize novel strains of Yarrowia lipolytica from artisanal Iranian dairy products such as kefir, yogurt, and different types of cheeses collected from various 62 regions and climates of Iran through phenotypic procedures and molecular techniques such as restriction analysis of PCR-amplified ITS-5.8S rDNA (ITS-PCR) and sequencing of D1/D2 domain of 26S rRNA encoding gene. One-way analysis of variance was used to compare the mean protein content, lipid production, biomass production, and lipid content in Y.lipolytica isolated strains. Crude protein determined by the Kjeldahl method.. Bligh and Dyer procedure were used for the extraction and quantification of yeasts lipids and Gas chromatography technique was used for the lipid quality assay.

Results: 19 isolates Yarrowia lipolytica are identified by Barcoding of the ITS and finally just 8 isolated confirmed as Yarrowia lipolytica by sequencing D1/D2 ribosomal DNA regions. The highest protein concentration of the biomass ranged was 56.21Â±2.3 % (w/w). The highest lipid content of 66.751 Â± 2.441% was attained by two isolated Y. lipolytica and the average amount of unsaturated fatty acids extracted from them was reached about 75% and they showed 80.382%, 80.079% of unsaturated fatty acids, including (72.7%), linoleic (C18:2) and oleic (C18:1) acid.

Conclusion: According to the results we can assess our isolated Y. lipolytica and recommended them for production purposes, including food and feed products based on biomass without any viable Y. lipolytica cells in the final product. In future study it is possible to couple the media engineering with this two candidate isolated strain of Y. lipolytica in order to optimize the biomass production in an optimized economical culture medium.

Keywords: Microbial food, ITS-PCR, 26S rRNA gene, Yarrowia lipolytica, Iranian dairy products.

Isolation of bacteriophage against Pseudomonas syringae pv. syringae in North-West of Iran (Research Paper)

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Introduction: Plant diseases caused by bacteria are a major economic liability to agricultural production. Disease control has been a major challenge for many bacterial diseases. There is a well-recognized need to develop new environmentally friendly control strategies to combat bacterial crop disease. Bacteriophages(phages), the viruses that infected bacterial cells, have received increased research interest in recent years as a realistic environmentally friendly means of controlling bacterial diseases. Their use presents a viable control measure for a number of destructive bacterial crop diseases, with some phage-based products already becoming available on the market. Phage biocontrol possesses advantages over chemical controls in that phage cocktails can be adapted to target speciï¬• c disease-causing bacteria. Unlike chemical control measures, phage mixtures can be easily adapted for bacterial resistance which may develop over time. In addition to phage cocktails, proteins produced by and isolated from bacteriophage have been investigated as alternatives to using complete and intact phage to treat crop infections. Pseudomonas syringae is a plant-associated bacterial species that has been divided into more than 60 pathovars, with the Pseudomonas syringae pv. syringae being the main causative agent of diseases in a wide variety of fruit trees.

Methods: Media : Nutrient broth medium (peptone 5 g; beef extract 3 g; NaCl 5 g per liter) was used as a broth or solidified with 1.8% agar (NA) to grow bacterial hosts. Soft agar for phage plaque-assays contained 0.9% agar. SM buffer (10 mM Trisâ€“HCl, pH 7.5; 100 mM NaCl; 10 mM MgSO4) was used for suspending and titrating the bacteriophages. Bacterial Strain: Bacterial strain used in this study is standard strain of Pseudomonas syringae pv. Syringae Bacteriophage Isolation: Phages were isolated from soil samples taken from Maragheh apricot orchard that had symptoms of the disease. The samples were treated as follows: 5 g of soil samples were mixed with 45 mL Sterile distilled water and centrifuged (3000Ã— g for 15 min at 4 â—¦C). The supernatant filtered through a 0.45 mm filter and mixed with 5 ml of nutrient broth and 5 ml of 4-hour culture of bacteria in nutrient broth and incubated for 18-24 hour in 37â—¦C. After incubation 3000 ml volume of chloroform was added to the mixture and incubated at 4 Â°C for 20 minutes then centrifuged (3000Ã— g for 15 min at 4 â—¦C). After filtration supernatant through a 0.45 mm filter, supernatant plated with the double layer agar technique. The phage titer (PFU/mL) was determined using a standard double layer agar.

Results: Phage isolated from soil sample and formed clear plaques on the host strain with a diameter of 0.3â€“1 mm. Phages were purified by successive single plaque isolation.

Conclusion: Food supplies from agriculture will need to intensify as a result of the anticipated growth in the human population. Phages and phage-based technologies are promising approaches for the treatment and biocontrol of bacterial diseases, including resistant pathogens. To fully implement phage-based applications, research into their efficacy in the real-world control of diseases in agriculture are needed

Keywords: Bacteriophages, biocontrol, Pseudomonas syringae pv. syringae

Knowledge domain of mRNA vaccines technology: A bibliometric assessment of research output (Review)

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Introduction: Messenger RNA (mRNA) vaccines are known as a relatively new vaccine class. This vaccine technology has indicated promising results for the future. This optimism is built on recently published studies demonstrating the efficacy of mRNA vaccines in combatting several types of cancer and infectious pathogens (such as coronavirus) where conventional vaccine platforms may fail to induce protective immune responses. These results would not have been possible without critical recent innovations in the field of biotechnology, such as the development of safe and efficient materials for in vivo mRNA delivery and advanced protocols for the production of high-quality mRNA. Therefore, this research conducted to review the scientific progress of mRNA-based vaccines via a bibliometric evaluation to identify the future perspectives.

Methods: In order to retrieve all the possible data, Web of Science (WoS) database considered as the data source of the present evaluation. Our search string contained "mRNA vaccine" and all its related keywords which were selected from Medical Subject Headings (MeSH) and other similar research projects. No limitations were considered for the language, region, and the publication date of documents. Bibliometric parameters were assessed by Biblioshiny R Package V3.1. Furthermore, co-occurrence analysis and visualizations were performed by VOSviewer v1.6.15.

Results: A total of 1247 documents were retrieved from WoS. Original articles (66.23%) and reviews (14.19%) were the most common document types. In total, documents on mRNA vaccines received 29971 citations. In results, the average citation per document was 24.03 (H-Index=71). The most international contribution was between the researchers from USA, Germany, and Italy by 419 (33.60%), 133 (10.66%), and 127 (10.18%) of the retrieved documents, respectively. In the case of prolific authors, Sahin U. with 25 (2.00%), Tureci O. with 18 (1.44%), and Weissman D. with 13 (1.04%) of documents were the most influential researchers by the number of publications. A review on journals indexed in WoS showed that among the journals hosting publications related to mRNA vaccines, Vaccines published the most significant number of documents 90 (7.21%). The co-occurrence network for keywords represented 3 publication clusters. The largest cluster was related to studies on the application and performance of mRNA vaccines in different aspects of deficiencies followed by studies on COVID-19 and viral diseases.

Conclusion: According to our results from WoS and VOSViewer, cooperation between countries, institutions, and authors were satisfying. We found that clinical trials on mRNA vaccines, and recently, immunoinformatical studies are

the research hotspots. The findings provided valuable insights into the scientific research progress in this domain and suggest scaling-up research and information dissemination on mRNA-based vaccines and vaccines safety. Based on the present results it is not unpredictable that research on the application of mRNA vaccines in different types of malignancies and also, other viral diseases continue during future decades.

Keywords: mRNA Vaccine, Scientometrics, Bibliometrics, Co-occurrence Network

KRAS inhibitors: A way for cancer treatment (Review)

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Introduction: Today, cancers become one of the major causes of death all over the world. Many processes, either endogenous or exogenous, play critical roles in cancer incidence and progression. By the way, endogenous mutant molecular pathways are known as the key to cancer pathogenesis in many studies. Kirsten rat sarcoma viral oncogene homolog (KRAS) gene is a proto-oncogene which mutations are among the most prevalent tumor drivers. Therefore, the present study is conducted to review the KRAS-G12C activity in cancer pathogenesis and the novel advances in cancer treatment by targetting this proto-oncogene.

Methods: A comprehensive search was conducted in electronic databases including Embase, Pubmed, Scopus, and Web of science with the keywords â€œCancerâ€□, â€œKRASâ€□ and all other related MeSH terms up to March 2022. Either original and review studies were reviewed to determine the KRAS-G12C activity, its role, and potential therapeutic agents in this proto-oncogene targetting.

Results: KRAS gene belongs to a member of the RAS family and its mutations are genetic drivers of multiple cancer types, including pancreatic ductal adenocarcinoma, colorectal cancer, and non-small cell lung cancer. In a detailed view, KRAS-G12 mutation is a predominant mutation in human cancers, and G12C is the most common mutation subtype in non-small cell lung cancer. In fact, KRAS protein is a signaling GTPase and provides a major signaling axis in tumor cell proliferation and survival which can be known as a key target for cancer treatment. Therefore, inhibiting KRAS, KRAS-G12C, can lead to cancer treatment by trapping the gene and its protein in an inactive GDP-bound state. The last discoveries in terms of finding the reliable KRAS-G12C inhibitor, Sotrasib were proved by FDA in 2021. The studies have been shown that despite KRAS-G12C inhibitor monotherapy can significantly treat some solid tumors, especially non-small cell lung cancer, but applying Sotorasib in combination with agents which target other oncogenic pathways and mediators such as mTOR, insulin-like growth factor 1 receptor, PI3K, ERK, EGFR can improve the therapeutic effects of the treatment regimen. Beyond the KRAS-G12C inhibitor, Sotorasib, resistance, the studies indicate the complexity of the genetic mechanisms of these reactions, which make us uncertain about whether the KRAS-G12C inhibitor resistance can frequently happen or not.

Conclusion: In conclusion, it can be stated that despite KRAS-G12C inhibitors, especially Sotorasib, which are known as a revolution in solid tumors treatment, there are some gray areas that need more investigations.

Keywords: Cancer, Solid tumors, KRAS, KRAS inhibitors, Sotorasib

Laparoscopic cholecystectomy in the treatment of gallstones (Review)

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Introduction: Background; The gallbladder is pear-shaped, located on the lower surface of the liver. The gallbladder is a storage site of fluid called bile that is made by the liver. Gallbladder stones are a relatively common disease in human societies and the definitive treatment for it is cholecystectomy. Which is performed by open and closed methods (laparoscopic) that the rate of general complications of laparoscopic cholecystectomy is less than the open method. The purpose of this review article is to evaluate the operation of laparoscopic cholecystectomy in the treatment of gallstones.

Methods: Research MethodØ› Relevant information was searched from Pub med, Scopus, Google Scholer databases; And data analysis was performed qualitatively.

Results: findings; Complications of Cholecystitis include infection within the gallbladder, death of gallbladder tissue, and gallbladder rupture. Usually, initial treatments include serum to prevent dehydration, use of painkillers to relieve pain, and so on. In some cases, it may be necessary to remove the gallbladder after initial treatment to prevent a recurrence, and one of the least common complications is laparoscopy, a type of surgery in which small incisions are made in the abdomen. After inserting a special instrument into the abdomen, they remove the gallbladder.

Conclusion: Conclusion; Studies have shown that laparoscopic is a safe and appropriate method for the treatment of all types of cystitis spots and can be used as the treatment of choice and the first line of treatment for cholecystitis.

Keywords: Keyword; Gallbladder, gallstones, cholecystectomy, laparoscopy

Liquid Biopsy: Alternative Technique for Tissue Biopsy (Review)

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Introduction: Cancer is a growing public health threat globally, becoming one of the leading causes of death worldwide. Hence, regarding the advances in instruments and technology in recent years, researchers have gone toward the approaches that facilitate the existing challenges in screening, target therapy, early diagnosis, and prognosis in cancer patients. This review discusses recent advances and future directions of Liquid Biopsy as an Alternative Technique for Tissue Biopsy.

Methods: This study was performed by using the collected article in English that was available on details of the main topic from 2000 to 2021 in Scopus, PubMed, Web of Science with keyword Liquid Biopsy, Cancer, tumor cell, CTC, Biomarkers. Articles were selected based on the exclusion criteria and were included in the study after reviewing.

Results: Tissue biopsies were the primary approach for these actions in the cancer field, which is still the most used. Although the current gold standard strategy in the area of actions against cancer typically involves the utilization of tissue biopsies, nevertheless the invasive nature of tissue biopsies causes many limitations, including sensitivity and accuracy, patient risk, sample preparation, procedural costs, and invasive testing. As a result, this method is incompatible with long-term clinical monitoring. Besides, one notable disadvantage of tissue biopsies is that they fail to detect intratumoral and inter-metastatic genetic heterogeneity, reducing the test's accuracy. Liquid biopsies have a great potential to overcome these current sampling limitations. Liquid biopsy is considered a minimally invasive and new technique for detecting tumor cells and identifying any tumor-derived products in various body fluids such as peripheral blood, saliva, urine, breast milk, and cerebral spinal fluid. These tumor-derived products include circulating tumor cells (CTCs), circulating tumor DNA (ctDNA), circulating tumor RNA (ctRNA), circulating tumor-derived proteins, extracellular vesicles (EVs), specifically exosomes and tumor-educated platelets (TEPs).

Conclusion: Overall, regarding numerous studies in recent years, liquid biopsies are promising tools for cancer-related implementations, including early-stage diagnosis, screening, minimal residue disease (MRD), targeted therapy monitoring, immunotherapy monitoring, and treatment response monitoring

Keywords: Liquid Biopsy, Cancer, Biomarkers, Early-stage Diagnosis, MRD

lncRNA DSCAM-AS1 regulates the P13K-AKT and Ras/Raf/ERK signaling pathway correlated to EPCAM in the breast cancer patients: integrated systems biology and bioinformatics investigation (Research Paper)

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Introduction: Breast cancer is the most common cancer and the leading cause of death among women1. The snail is a crucial regulator of tumor cells' epithelial-mesenchymal transmission (EMT). Several studies have shown that nuclear snail expression is an adverse prognostic factor in human cancer2. Differential expression analysis was performed on the microarray datasets to find significant irregular genes in breast cancer cell line MCF.7. In this study, 54,675 genes were analyzed. After performing the Limma closed linear model on expression data, 5239 low-expression genes and 4697 high-expression genes were identified in this study, which was selected for bioinformatics and subsequent experimental research. This analysis illustrated that mRNAs have a single local base-pairing interaction, miRNA interaction analysis revealed that could regulate the expression of mRNA and lncRNA in an interaction axis, and we also show strong interactions between miRNA and lncRNA and selected genes.

Methods: GSE58252 dataset Affymetrix was chosen and analyzed to find differentially expressed genes (DEGs) in BC samples compared to control samples. The GEO online database was used to find this dataset. The limma was used to conduct the DEG analysis. 6 samples were evaluated (3 controls and 3 patient BC samples). The genes with logFC > 2 & logFC < -2 are considered as the differentially expressed genes (DEGs) in this dataset. The adjusted p-value (adj. P. Value) < 0.001 is considered as the statistical significance level. The miRWalk was used to analyze miRNAâ€“mRNA interactions. The Pathway enrichment analysis was carried out using KEGG and Reactome's online databases. All miRNAs were regained from DIANA-TarBase v7.0. The expression of lncRNAs in different tissues has been examined by the lnCAR databases. I was comparing the expression of genes in Breast cancer by Gepia2 databasesâ€”the protein-protein interaction analysis by STRING online software.

Results: We examined three genes including KRAS, EPCAM, and DSCAM_AS1 (logFC > 2 & logFC < -2, adjusted p-value (adj. P. Value < 0.001) is considered as the statistically significance level. we found that mRNA EPCAM and DSCAM_AS1 lncRNA expression was increased, and mRNA KRAS decreased in tumor tissue from breast cancer patients compared to healthy patients. DSCAM-AS1 has significant direct interactions with the KRAS

and EPCAM mRNA in Breast cancer cell line MCF.7. KRAS and EPCAM had several significant interactions that Played an important role in regulating cell proliferation. Interaction analysis of EPCAM, KRAS mRNA, and DSCAM_AS1 lncRNA illustrated that these RNAs have a single local base-pairing interaction (Energy = -36.43 kcal/mol) and (Energy = -12.01 kcal/mol). miRNA interaction analysis revealed that hsa-miR-373-3p could regulate the expression of EPCAM and LINC01018 lncRNA in an interaction axis. In addition, hsa-miR-183-5p could regulate the expression of KRAS and ADAM1A lncRNA in an interaction axis. KRAS could regulate the following signaling pathways: Ras, Breast cancer, Proteoglycans, MicroRNAs signaling pathway in cancer in cancer.

Conclusion: KRAS, EPCAM, DSCAM_AS1 could be three prognostic biomarkers. lncRNA DSCAM_AS1 expression level has a significant positive correlation with the expression of KRAS and EPCAM in breast cancer; KRAS plays a role in the RAS protein in the MCF.7 cell line in breast cancer in the MAPK signaling pathway, which plays an essential role in proliferation furthermore in P13K_AKT signaling pathway can regulate the CELL proliferation Angiogenesis DNA repair. EPCAM knockdown led to decreased phosphorylation of Raf and ERK, suppression of malignant behavior of breast cancer cells, and inhibition of the Ras/Raf/ERK signaling pathway3.

Keywords: Breast cancer, Snail, EPCAM, KRAS, MCF-7, DSCAM_AS1

Magnetotactic Bacteria: From Magnetic Navigation to Biomedical Applications (Review)

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Introduction: The physicist William Gilbert was the first scientist about 420 years ago that described the earth as a giant magnet affecting magnetic objects on its surface. He designed the experiments that showed the positional changes of the direction magnetic needle under the gradient of the earth's magnetic field along the horizontal and vertical axis. Hence, he proved the difference in the gradient of the earth's magnetic field. Despite many endeavors to find a sense of cognitive magnetism in vertebrates, scientific experiments in this field have been fruitless. It is obligatory to deeply understand the molecular mechanisms of the phenomenon in some model organisms, such as bacteria, that can introduce them as a magnetic unit of life. Magnetotactic bacteria are microaerophilic or anaerobic bacteria that can detect magnetic field lines and migrate to the sediments and anaerobic areas having the optimal conditions for their growth by using their flagellum. The phenomenon is mostly known as "magnetotaxis". This characteristic indicates the existence of a different organelle or cell structure than other bacteria, called magnetosomes. Magnetosome is an intracellular organelle synthesized by the magnetotactic bacteria that enables them to detect the magnetic field lines of the earth so that they are still able to orient in the magnetic field even after death. This cellular substructure consists of an organic component (phospholipid bilayer membrane) and an inorganic element (mineral magnetic nanoparticles), the inner space of which is usually occupied by a mineral iron crystal of iron oxide (Fe3O4), iron sulfide (Fe3S4), or pyrite (FeS2). Fe3O4and Fe3S4, also called magnetite and greigite, respectively, have elevated magnetic properties but FeS2 lacks magnetic properties, known as a diamagnetic compound. Although these crystals are morphologically diverse, both types of nanoparticles are composed of a lipid-bilayer membrane containing unique proteins. The size of the magnetosomes is in the range of 35-120 nm. According to the emphasis of nanoscience on efficiency of nanoparticles with dimensions less than 100 nm, these nanoparticles have a high potential for utilization in various industries. Most of the magnetosomes are chained or scattered around the longitudinal axis of the cell. â€ƒ The number of magnetosomes varies in the different types of magnetotactic bacteria. For instance, the average number of nanoparticles per cell is about 17.6 in MS-1, as the magnetite type nanoparticle. Besides, the distance between the surface of the nanoparticles and the magnetosome membrane is 1-6 nm and the magnetosomes are spaced about 3-18 nm. In â€˜Candidatus Magnetoglobus multicellularisâ€™, there is an average of about 80 magnetosomes (up to 180 nm) with greigite nanoparticles per cell. Mineral

of most magnetosomes is magnetite, however, some magnetotactic bacteria contain greigite nanoparticles, and also, there is a known type of bacteria that synthesizes both nanoparticles. The structure and composition of elements, shape, and size of magnetosomes can be studied using high-resolution transmission electron microscopy (HRTEM), energy dispersive X-ray analysis (EDXA), scanning X-ray fluorescence microscopy (SXFM), and nanoscale X-ray absorption near-edge structure (nano-XANES). The mineralization process of magnetosomes is a highly regulated process in which their morphology, composition, and size are directed and controlled at the gene expression levels. The mineral processes for the construction of the nanoparticles in magnetosomes are genetically controlled by a group of genes in magnetotactic bacteria. More than 30 genes are involved in the synthesis of magnetosomes. For example, in the Magnetospirillum gryphiswaldense MSR-1 (MSR), magnetosome genes are organized into five polycistronic operons, including mms6, mamXY, mamAB, mamGFDC, and feoAB1. The production methods of magnetosomes include biosynthesis and laboratory synthesis by genetic engineering techniques. Biosynthesized nanoparticles possess greater advantages over synthetic magnetic ones, including biocompatibility, purity, and excellent magnetic properties. Magnetosomes have engrossed a highly consideration in magnetic resonance imaging (MRI), hyperthermia, drug delivery, cancer theranostics, gene therapy, biomedicine, tumor detection, biosensors, and enzyme immobilization.

Methods: Review paper

Results: Review paper

Conclusion: Discovery of the Earth's magnetic field, importance of finding the origin of magnetic properties in living organisms, and also, the growth and development of nanotechnology and its applications in various industries have highlighted magnetotactic bacteria among the others. Magnetotactic bacteria have a unique subcellular structure called magnetosome consisting of a magnetic nanoparticle of magnetite (Fe_3O_4) or greigite (Fe_3S_4) mineral with the dimensions of 30-120 nm and a lipid-bilayer phospholipid coating, which replace them with synthetic magnetic nanoparticles. Magnetosomes have been highly considered as the intelligent and safe carrier for targeted drug delivery, purification of macromolecules, biosensors, and hyperthermia, due to having high purity magnetic nanoparticles and lipid-bilayer membrane with proprietary proteins.

Keywords: Magnetotactic bacteria, Magnetosomes, Magnetic field, Magnetic nanoparticles, Biomineralization

Making antiviral (against IBV) nanofibres based on electrospinning method, using polyacrylonitrile and polyvinyl alcohol polymers with copper salt and copper nanoparticles for mask filter production (Research Paper)

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Introduction: The connection of nanoscience with biology not only helps to fight diseases, but can also create a new approach to preventing and fighting infectious diseases(1). Recent studies in the field of nanotechnology show that nanoparticles of various metals can be widely used against microorganisms and even fungus(2, 3). One way to perform antiviral tests using embryonated chicken eggs(4). Aim: The purpose of this study was to fabricate antibacterial and antiviral activity of nanofibers that use nanoparticles and copper ions.

Methods: To make nanofibers, a solution of polyacrylonitrile 15% and polyvinyl alcohol 20% (with gelatin) is used simultaneously using two separate syringes. These nanofibers are made of 9 ml of polyacrylonitrile in the first layer, 4 ml of polyacrylonitrile and 4 ml of polyvinyl alcohol in the second layer. The applied voltage is 23 kW and the drum speed was set to 600 rpm. The electrospinning process is performed by applying 285 nm UV rays. The produced nanofibers were impregnated with copper sulfate solution prepared in a ratio of 1:3. They were then imaged with a SEM electron microscope. In the next step, the fibers are affected by plasma processing for 30 seconds. Copper sulfate solution is then added to these fibers. To check the antimicrobial properties of the fibers, the next step is to perform microbial tests to ensure that bacteria and fungi do not grow. For this purpose, nutrient broth and tryptic Soy Broth culture medium for aerobic microorganisms and thioglycolate Broth culture medium for anaerobic microorganisms, were used. Then incubated in a 37Â°C incubator for mesophilic microorganisms and in a 45Â°C incubator for thermophilic bacteria for 72 hours. In the next step, with a wet soap, samples taken from the surface of the fiber and place it in Blood agar culture medium and incubated for 72 hours to check the growth of microorganisms. In antiviral studies, various factors are considered. In the first stage, the effect of plasma and UV processing on the antiviral properties of nanofibers investigated. The number of particles of IBV and the effect of copper ions on them are also observed. In the second part, the appropriate concentration of copper for the survival of embryos and its effect in combating IBV are investigated. Embryonated chicken eggs are ready for inoculation on the twelfth day. In the first stage, the IBV, which is used as a commercial Live-attenuated vaccine (Bioral), each dose contains 103 virus. The PCR test used to detect the genome of IBV in treated and control samples.

Results: The results of antibacterial test shown that fibers impregnated with copper sulfate solution and exposed to UV radiation and plasma processing could resist the growth of aerobic, anaerobic, mesophilic and thermophilic microorganisms and prevent their growth. The results of the first antivirus test show that nanofibers that are not affected by plasma processing show better results than nanofibers that are not affected by plasma processing. Under these conditions, fewer embryos have died due to copper toxicity. On the other words, the virus had a greater impact on embryos growth, and nanoparticles and copper ions in normal nanofibers were able to prevent the virus to a greater extent. The PCR results showed that treated samples did not form a band compared to the positive control samples. This means that the virus inactivated. In the second part of the antiviral tests, the best results is obtained in a set in which the initial solution of copper sulfate is diluted at 1/16.

Conclusion: Prepared nanofibers containing nanoparticles and copper ions demonstrated designated antibacterial and antiviral activity that implies such a product can be used in respiratory filtered mask widely.

Keywords: Nanofiber, Antiviral, Copper sulfate, Nanoparticles

MDC1-AS1 lncRNA expression in glioblastoma (Research Paper)

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Introduction: Background and purpose: Glioblastoma is one of the most malignant and common brain tumors, accounting for about half of all gliomas. Glioblastoma is a tumor of the central nervous system (CNS) that originates in the glial tissue of the brain. The aim of this study was to investigate the changes in the expression of lncRNA 1 MDC1-AS as a possible biomarker in glioma.

Methods: For this purpose, after reviewing the medical records of patients at Imam Hossein Hospital in Tehran, obtaining written consent from patients and code of ethics in Imam Hossein Hospital was performed. Paraffin blocks including brain tumor biopsy from 1394 to 1396 were collected and by The pathologist was confirmed and the degree was determined. In this project, 50 samples of grade 1 and 2 and also 50 samples of grade 3 and 4 were examined. For all tissue samples donated by patients, RNA extraction and cDNA synthesis were performed and then a specific primer and probe were designed and the expression level of MDC1-AS gene 1 using the technique Real-time PCR was evaluated. The mean age of the subjects was 43.70 16 16.416 years. Statistical analysis was performed descriptively and analytically using SPSS Ver20 software and unpaired Sample Student T Test was used to compare the amount. Expression of this gene was used in lower grade tumor tissue and higher grade tumor tissue.

Results: The results showed that tumor samples with grade three and four had 0.202 times more expression (fold change) than tumor samples with grade one and two. And this distance is statistically significant

Conclusion: The results of quantitative study showed that MDC1-AS1 gene expression decreased significantly with increasing disease degree (with P-value = 0.0001).

Keywords: Glioblastoma, lncRNA, 1 MDC1-AS1

Metabolic stressors stimulate the co-production of multiple high-value compounds accumulation in cyanobacterium Arthrospira (Review)

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Introduction: Microalgal cultivation, as a green technology, has now received great attention. The biomass of cyanobacterium Arthrospira (i.e., Spirulina) studied as superfoods owing to contain about 50-70% protein, 15-25% carbohydrates, and 6-13% lipids, as well as substantial amounts of vitamins, minerals, and pigments (Phycocyanin, chlorophylls and carotenoids) which make the Arthrospira of excellent nutritional profiles and high-quality proteins (Salla et al. 2016; Fekrat et al. 2018). However, Arthrospira shows potential for being used as ingredients in the development of novel functional foods, which are among the top trends in the food industry (Lafarga et al. 2020). In the meantime, the suitable cultivation conditions for high-value compounds hyperaccumulation are the most challenging approach in Arthrospira platensis. However, to date, limited studies have been reported with respect to exploring various strategies for the co-production of multiple compounds in Arthrospira platensis. Arthrospira cells can simultaneously accumulate various valuable compounds; thus, the co-production of multiple products is achievable.

Methods: For the co-production of multiple metabolites in marine microalgae, numerous cultivation strategies have been using based on environmental conditions (Temperature, Salinity, Light), nutrient conditions (Nutrient sufficient/Deficient strategy, Semi-continuous/ Fed-batch strategy) and multiple factors integrated strategies (Two-stage cultivation with a combination of different Parameter) can be explored to enhance the co-production of multiple compounds (Ma et al. 2020).

Results: Arthrospira, with a flexible tricarboxylic acid (TCA) cycle, is an appropriate candidate for co-production of valuable metabolites by using metabolic stressors. The biosynthesis of lipids, pigments, carbohydrates, and proteins, is highly interconnected in the metabolic network and controlled by limiting steps. Metabolic flux may shift to different metabolites under specific cultivation conditions. Exploring novel cultivation strategies by integrating environmental and/or nutrient factors can be an effective way to improve the co-production of multiple compounds. Metabolic stress is a promising approach for metabolic pathway manipulation and elevation of interest metabolites production and cell growth. The TCA cycle is unusual and incomplete in cyanobacteria due to missing the 2-oxoglutarate dehydrogenase (OGDH) enzymes, and several shunts are identifiable. The GABA shunt is a variant of the TCA cycle that utilizes glutamate decarboxylase to convert glutamate to GABA. Then, GABA aminotransferase (GABA-T) converts GABA to alanine, and alanine aminotransferase (AlaAT) converts alanine to pyruvate and vice versa (Steinhauser et al. 2012). These findings revealed that GABA is one of

the main components providing carbon for the TCA cycle and increasing lipid production in microalgae under abiotic stress conditions (Zhao et al. 2020). Hence, it seems that the level of pyruvate can be affected by the GABA shunt pathway. Further, an increase in GABA and alanine levels in the GABA shunt pathway probably can affect fatty acids and other metabolites induced. The aspartate transaminase reactions are the other critical variant pathways in cyanobacteria (the AspAT shunt), which permit the recycling of metabolites (Steinhauser et al. 2012). Aspartate aminotransferase is considered a critical enzyme for biomass production catalyzing the reversible reaction of 2-oxoglutarate, glutamate, aspartate, and oxaloacetic acid produced by the TCA cycle, linking nitrogen assimilation with carbon metabolism (Ghaffari et al. 2016). It also seems via the citrate-malate shunt that oxaloacetate is converted to pyruvate by oxaloacetate decarboxylase, which is a precursor to acetyl coenzyme A (Acetyl-CoA). Likewise, Acetyl-CoA. is a precursor for producing fatty acids and carotenoids. It has been evidenced that the classic TCA cycle produces energy agents (i.e., NADH & FADH) and biosynthetic precursors (for producing amino acids, lipids, and â€œhemeâ€• synthesis and linking to nitrogen metabolism), whereas the variants with their oxidative and reductive branches generate more biosynthetic precursors (AraÃºjo et al. 2014).

Conclusion: Different patterns of desired metabolic profiles are easily attainable with some minor changes in growth conditions and/or medium compositions of cyanobacteria. More studies are needed to understand the key metabolic checkpoints and regulatory sites in primary intermediate metabolites utilized in Arthrospira. The presented strategy seems to provide an eco-friendly approach for reducing the production cost of biomass and valuable metabolites in A. platensis.

Keywords: Arthrospira platensis, Co-Production, metabolites, metabolic stress, TCA cycle

Molecular immunology using nutrition and its association with cancer (Review)

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1.

Introduction: Nutrition is one of the most important ways to prevent diseases. By using nutrition, molecular immunology can be increased and also various diseases, especially cancer, can be prevented. The lymphoid system is widely localised in the gut and those cells are particularly sensitive to metabolites induced from nutrients and products induced from microbiota and they also modulate the activation and function of the cells. Approximately 70% of the cells in the immune system and over 90% of the Ig producing cells in human body are localised in the intestines. Nutrition and immunity are closely related. The immune system composed of the most energy-consuming cells in the body. Therefore, they are strongly affected by imbalance of the nutrients. Immune system cells use glucose, fats and amino acids as a source of energy. The homeostasis of innate and adoptive immune system cells is greatly influenced by the circulating fatty acids. Fatty acids are a source of energy for immune cells, and a structural component for phospholipids and membrane structure. Depending on their role in one-carbon metabolism and protein synthesis, methionine (egg, cheese, fish) is effective in the activities of immune system cells. Vitamins and minerals are key dietary components and also influence the function of the immune system cells. Based on in vitro and in vivo studies, the present article examines the effects of vitamins and minerals that may affect the functions of immune system cells in patients receiving cancer treatment. Also Leptin is a hormone released from adipocytes. It has been shown that nutritional status, metabolism, the energy level in adipose tissue are very important for the relationship between immunoresponse and leptin. Epigenetic has been described as inherited mitotic and potentially reversible changes with DNA sequence and molecular modifications in chromatin structure and non-coding RNAs, microRNAs. According to a growing number of studies in the nutriepigenetic field, expressions of genes related with the development and functions of immune cells are regulated by vitamin B12, B1 and folates. A large majority of nutrients (fats, proteins, vitamin E, C) control expressions of specific microRNA (miRNA/miR). Unsaturated fatty acids inhibit the expression of miR-21, miR-122a and miR-125b in mice and humans, and they regulate Th2 response in myeloid cells by the inhibition of IL-12. The inhibition of histone deacetilases (HDACs) is related with the anti-inflammatory function of butyrate. It was demonstrated that HDAC inhibition regulates the macrophage function and T-reg cell development. Vitamins such as biotin, niacin, pantotenic acid etc. Therefore, in this article, we examine molecular immunology through nutrition and cancer prevention.

Methods: This article was conducted using library research method. We used reliable sources and related books and articles to collect information.

Results: After investigations, we found that cellular stress may be of pathogenic, nutritional, oncogenic or physical origin. Cellular stress includes principal reflection, such as response to DNA damage, tumor suppressor genes and activation of aging.

Conclusion: In contrast, the secondary response to cellular stress is the activation of immune system, and natural killer cells (NK) may indirectly activate the immune system. However, intrinsic responses can directly activate the immune system; and it was also demonstrated that some chemotherapies could not be effective without the presence of an immune system.

Keywords: Immunology, Molecules, Nutrition, Cancer

Nanotechnology and Drug Delivery in the Renal Cancer (Review)

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Introduction: The renal (kidney) system functions as a blood filter. Renal cortical tumors can be malignant, benign, or indolent. Renal cancer is a complex disease that necessitates the use of multitarget inhibitors (MITs) to address issues such as resistance development. The drugs utilized are both single-drug inhibitors (SDI) and multi-drug inhibitors (MDI). Because there is currently no cure for metastatic RCC, nanotechnology can only be used in a limited way. Traditional drug delivery methods harm both cancer cells and healthy cells, necessitating the development of specific active and passive drug delivery strategies. Renal cancer pathogenesis is complicated and diverse, impacted by many factors, including smoking, obesity, workplace exposure, genetic and hereditary risk factors, gene mutation (inherited or acquired), and the presence of von Hippel-Lindau disease, to name a few. Birt-Hogg-Dube (BHD) syndrome, hereditary papillary renal cell cancer, hereditary leiomyoma-renal cell carcinoma Renal cancer in the family, hereditary renal oncocytoma, a family history of kidney cancer, and high blood pressure are all factors to consider. Nanoparticles interact with cells and tissue in different ways. Nanoparticles can be employed as a medication delivery vehicle for both targeted and controlled drug release (timed release or single-dose injection). Antibodies, nucleic acids, proteins, and peptides, which are required for targeted medication administration, can also be delivered to the site of action by nanoparticles. Overdosing, adverse effects and injury to healthy cells are all avoided. The purpose of this research is to study nanotechnology and drug delivery in renal cancer.

Methods: This study was the study of nanotechnology and drug delivery in renal cancer, that was by searching scientific databases such as Google Scholar, PubMed, Science Direct, Springer.

Results: The result showed Use of nanotechnology for delivering drugs to renal cancer is still in its infancy. The glomerular capillary wall is a structure in the kidneys that filters blood. Nanoparticles with a diameter of less than 10 nm are subjected to first-pass renal filtration, hence their size is critical. The findings revealed that particles larger than 100 nanometers in diameter can aggregate in tumor tissue while being passively targeted and that this accumulation is solely dependent on diffusion-mediated transit into the tumor. Stable nanoparticles in circulation for longer periods result in increased drug uptake by tumors and less toxicity by avoiding the reticuloendothelial system. Nanocapsules, Nanospheres, Micelles, Nano-Liposomes, Dendrimers, and others are examples of successful nanoparticles in drug delivery. Pharmacokinetic and pharmacodynamic studies in pathological circumstances with substantial decreases in glomerular filtration are the focus of kidney-targeted medication delivery. To target medications to the glomerulus,

mesangial cells, and medium fibroblasts, new nanocarriers are being developed.

Conclusion: To summarize, nanotherapy for renal cancer is still in its early stages. The multifactorial nature of cancer and renal clearances, as well as the occurrence of many different forms of renal cancer, are substantial roadblocks. Different types of nanoparticles are evaluated for their suitability as medication carriers. Minimize the buildup of any non-biodegradable polymer or other nanoparticles (used in drug delivery) with a size greater than the renal threshold size 31, and prevent nanoparticles from crossing the BBB are two factors that should not be overlooked. Another question that has been raised is whether nanotechnology can aid in the treatment of metastatic cancer, which contains extremely small cells, a high multiplicity, and is scattered throughout several organ settings. Only timely diagnosis holds out hope soon. Due to the multifarious origins of cancer, delivering medications to various organs may need a significant amount of study. The future will benefit from a combination of nephrology, medicine, and nanotechnology to develop target-specific, safe, and cost-effective nanomedicine for renal illnesses.

Keywords: Renal Cancer; Tumor; Nanotechnology; Drug deliver

NcRNAs as therapeutic target for diabetes and its complications (Research Paper)

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Introduction: Diabetes is one of the most common metabolic diseases that leads to the induction of many health complications. In developed countries, it is the main cause of blindness, end-stage renal failure and non-traumatic amputation of the lower limbs. Diagnosis and treatment progression have key role in exploration of biomarkers for diabetes. A novel group of gene expression regulators is a class of small non-coding RNAs of 18-24 oligonucleotides in length, function to post transcriptionally regulate protein expression termed ncrRNAs which can cause gene silencing through degradation of target mRNAs or blocking of translation. Dysregulated expression of ncRNAs include microRNAs (miRNAs) and Long non coding RNAs (lncRNA) has been shown in various human diseases, such as diabetes.so this study aims to investigate the relationship between diabetes and ncRNAs in associated pathways.

Methods: By using mirbase, HMDD and miRdSNP, miRNA properties were obtained. The miRTarBase, MIRWALK2.0 and TargetScan, target genes were identified. Venn diagram used to identify common target genes between MiRNAs. Using DAVID and KEGG, signal paths were obtained and the pathways associated with diabetes were interpreted. The gene network was obtained through GENE MANIA.

Results: We identified hsa-miR-23a-5p as the best miRNA, its target genome and associated cell signaling pathways. Then, the findings presented that this miRNA had a key role in polyol pathway, hexosamine pathway, PKCs signaling, oxidative stress, AGEs pathway, PARP pathway, MAPK pathway, NF-Î°B signaling, hedgehog pathways, TNF-Î± signaling, cyclooxygenase pathway, interleukins, lipoxygenase pathway, nerve growth factor, Wnt pathway, autophagy, and GSK3 signaling that may be accounted for the pathogenesis and progression of diabetic. Next, we used series of bioinformatics software to obtain the lncRNAs and their relationship with over expression gene and diabetes.

Conclusion: : Diabetes is a complicated and life-threatening disease, which affects â^¼30-90% of diabetic patients across the world. Multiple signaling pathways are integrally accountable for the development and pathogenesis of diabetes. The result demonstrated that has-mir23a-5p inhibits Ras by blocking Raf-1, MEK1/2 which active ERK, SRF and c-fos through phosphorylation in MAPK and Gap junction pathways. Mentioned microRNAs prevent allergic

asthma by inhibiting (IL1b-IL6-IL15-lif-tnf) by blocking MKK4/7, JUNK1/2 in TNF pathway. The long non-coding RNA metastasis associated lung adenocarcinoma transcript 1 (MALAT1) is highly phylogenetic and conserved in mammals. MALAT1 knockout decreased the expression levels of total and phosphorylated p38 and reduced the apoptosis of rat CEP cells. The results obtained in the present study indicated that MALAT1 may serve as an important therapeutic target for diabetic patients. This new molecular methods for the accurate treatment of diabetes is suggested.

Keywords: Diabetes, MAPK pathway, MicroRNA, TNF pathway, LncRNA

Novel effect of Arthrocen (avocado/soy unsaponifiables) on pentylenetetrazole-induced seizure threshold in mice: Role of GABAergic pathway (Research Paper)

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Introduction: Arthrocen, an avocado/soy unsaponifiable (ASU)-containing agent, is used in the clinic and it can decrease the pain of joint potentially. Inflammation and pain associated with mild to severe osteoarthritis. Phytosterols are the major component of Arthrocen with documented anti-inflammatory properties, antioxidant, and analgesic effects. Here, we evaluated ASU anticonvulsant effect by its oral administration in pentylenetetrazole (PTZ)-induced seizure threshold and Maximal Electroshock Seizure (MES) Models. Also, the involvement of N-methyl-D-aspartate (NMDA) receptor, benzodiazepine receptor, and nitric oxide (NO) pathway were studied in anticonvulsant effect of ASU in male NMRI mice.

Methods: Acute administration of Arthrocen (10, 30, 75, 150 mg/kg) by oral gavage significantly (pâ€¯<â€¯0.01) increased the clonic seizure threshold induced by intravenous administration of PTZ.

Results: Nonspecific inducible NO synthase (NOS) inhibitor L-NAME (10 mg/kg) and a specific NMDA receptor antagonist MK-801 (0.05 mg/kg) did not affect the anticonvulsant effect of Arthrocen, while pretreatment with flumazenil (0.25 mg/kg), a selective benzodiazepine receptor antagonist, reversed this effect (pâ€¯<â€¯0.01). Also, Arthrocen treated mice did not affect tonic hindlimb extension in the MES model. The data demonstrated that Arthrocen could probably produce its anticonvulsant effect by enhancing GABAergic neurotransmission and/or action in the brain.

Conclusion: To conclude, the results of this study illustrate that Arthrocen had anticonvulsant property in PTZ-induced seizure threshold. This activity could not be reversed by NO inhibitor and NMDAR antagonist, but the GABA-A receptor antagonist could completely block the anticonvulsant effect of Arthrocen. Our findings reveal that GABA-A receptor may be contributing to the anticonvulsant effect of ASU.

Keywords: Arthrocen; GABA-A receptor; Nitric oxide synthase inhibitors; Pentylenetetrazol.

Novel solution for Cancer treatment problems; Combination of Oncolytic virotherapy and Immunotherapy in cancer treatment (Review)

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Introduction: Oncolytic viruses (OVs) show a new class of therapies that utilizes replicable viruses to cure various types of cancers. Up to now, common oncolytic viruses have been comprised of herpes simplex virus type 1 (HSV-1), oncolytic adenovirus, Newcastle disease virus, oncolytic smallpox virus, and Rhinovirus.

Methods: The main attraction to oncolytic viruses (OVs) was as a method of treating cancer based on their distinctive features such as selective tumor proliferation and specific cell toxicity. OVs selectively infect cancer cells and use the host cell apparatus for direct proliferation and lysis of tumor cells.

Results: Tumor cell lysis releases tumor-specific antigens that stimulate both the innate immune system and the adaptive immune system. OVs are able to reverse some of the carcinogenic effects and increase antigen processing and delivery, T cell activation, trafficking, and killing, and finally have powerful immunotherapeutic efficacy.

Conclusion: The problem with oncolytic virus therapy is the risk of uncontrolled proliferation in vivo. Combining oncolytic virus therapy with other anti-tumor therapies, including chemotherapy and radiation therapy, as well as cancer immunotherapy can be used to target a wider range of tumors and enhance therapeutic efficacy. The combined approach of an oncolytic virus and a PD-1 or PD-L1 blockade can increase antitumor immunity and oncolytic effect. The combination of oncolytic virus therapy and CAR-T immunotherapy has a synergistic effect in cancer patients.

Keywords: Ocolytic viruses, treating cancer, CAR-T immunotherapy, cancer patients

Phage based vaccines: Methods, formats, and efficacy an overview (Review)

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Introduction: Bacteriophages (simply called phages) are known as viruses that seize bacteria, these virus particles were first identified by Frederick Twort and Felix d'Herelle in 1915 and 1917 respectively. Phages are the most manifold organism on earth. These virus particles can cause infection in their specific bacterium host and do not damage another organism but they can trigger the innate and adaptive immune systems in nonâ€“bacteria organisms. Many studies indicate that phages have high potential in genetic engineering especially filamentous ones by the way this high potential convinced scientists to use these viral particles in many biotechnology applications such as vaccine design, cancer therapy, and drug delivery. In this study, we try to examine the methods of phage base vaccine creation and introduce novel studies which use these types of vaccines against infectious diseases and some types of cancer.

Methods: 1- Article searching was performed by using Phage display, phage-based vaccine, and phage genome engineering as keywords at PubMed and Science direct. 2- Publication date was set on last 5 years at each website 3- The literature involving vaccine designing, phage display, and related studies were selected for further studies 4- Both review and original articles and also editorial book used to gain data for this study

Results: 1477 and 9843 results were found in PubMed and Science direct respectively after searching related keywords. The results were reduced to 370 and 2061 after applying the last 5 years' filter. At last after the criteria check of results 59 items were selected for further studies. 2- phage-based vaccines format These types of vaccines are set up in two specific systems: phage DNA vaccines and phage display vaccines. Briefly in phage DNA vaccines phage work as a delivery system to hand over a DNA vaccine to the desired cell, in the other hand phage display vaccines known as transgenic viral particles which expressed immunogenic peptides or proteins on their surface. However, the capability of bacteriophage T7 in the combined use of these two formats in a single particle was shown recently. The most abundant type of phages that are used in vaccine design includes T4 phage with Hoc and Soc proteins used for display and also Î» bacteriophage with gpD proteins, T7 bacteriophage with gp10B proteins, MS2 bacteriophage with CP proteins, QÎ² with A1 proteins M13 with PVIII and PIII proteins. 3- phage-based vaccines that show good function against disease or cancer Î» bacteriophage against BALB/c TUBO mice model. M2e-Displaying T7 Bacteriophage against Influenza A Virus T4 Vaccine Platform against influenza Bacteriophage QÎ² against HIV-1 Bacteriophage based vaccine against SARS-Cov 2 Bacteriophage T4 against Anthrax and Plague Bacteriophage T4 against murine transplantable colon carcinoma 4- methods uses for genetic engineering of phages Methods for this purpose are divided into two types, genetic methods and chemical methods. 4-1- Genetic

methods: the traditional method cause Homologous Recombination that based on using two different phages to infect a single bacteria cell or homologous recombination between the plasmid and wild-type phage genome Bacteriophage Recombineering of Electroporated DNA (BRED) this method was firstly described by Marinelli et al and based on using electroporation to enhance the possibility of intaking wild type phage and donor plasmid by bacteria CRISPR â€“ Cas technology Reconstruction of phages into the host cell by transforming the assembled DNA in host bacteria New combined methods e.g CRISPY-BRED and CRISPY-BRIP were applied in recent studies. 4-2- The chemical methods include Amine group modification by NHS, Sulfo-NHS, incorporated NHS with PEG, and Tetrafluorophenyl (TFP) esters. Carboxylate Group modification by the water-soluble 1-ethyl-3-(3-(dimethylamino)propyl)-carbodiimide hydrochloride (EDC) or water-insoluble dicyclohexylcarbodiimide (DCC) and addition of NHS esters. Thiol group modification by Maleimides. Phenol group modification by diazonium compounds. Using Aldehyde Cross-Linkers e.g Glutaraldehyde.

Conclusion: Vaccines are the most important weapons of the human race against infection diseases, thus designing the vaccines with high efficacy, safe enough for mass use, and also with fewer side effects can ensure the survival of humanity. Most of the studies indicate that the phage-based vaccine is a reliable tool to fight against cancer and infection disease, in addition, phages are safe because they are unharmed to non-bacterial cells, and they have fewer side effects in comparison with other virus-based vaccines.

Keywords: Phage display, phage-based vaccine, phage genome engineering

Platelet-derived factor and regeneration medicine (Review)

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Introduction: Human platelets lysate (HPL) is a cell-free biological substance, rich in protein, growth factor, cytokines, and chemokines, which is mainly produced from obsolete human platelet concentrates and is used in cell growth and proliferation. It is also a good alternative to bovine fetal serum and bFGF. These cells do not stimulate tumor growth in the body, and having human origins reduces the safety and infectious concerns of bovine-derived substances. Platelet lysate (PL) has more growth factors and is cheaper and easier than other hemoderivative agents, but because the half-life of PL is short and the variety of growth factors between different donors is high, the clinical application of PL is limited. It is difficult to maintain PL and growth factors in the tissue because they dissolve in the blood a few days after injection. PL is used clinically in surgical treatments for soft and hard tissue defects and in wound healing, bone regeneration, alopecia, oral mucositis, radiculitis pain, osteoarthritis, eye diseases.PL is also used in cell culture and for transplantation purposes.

Methods: This article is an overview of platelet lysates and their applications in biotechnology. The search was performed by combining the keywords platelets, platelet lysates, biotechnology, blood products, etc. in various databases such as Science Direct, Google Scholar, and PubMed. Our searches have been from 2020 to 2022 and newer information has been considered. The result of at least 30 articles was extracted by each researcher individually and discussed. Finally, the data collected by the authors were analyzed, shared, edited, and critiqued if necessary.

Results: Studies show that HPL can be more beneficial than PRP because it does not block blood vessels. HPL is currently the most promising human cell culture replacement supplement for FBS and has been used for mesenchymal and endothelial progenitor cell proliferation for more than a decade. Studies show that HPL can be more beneficial than PRP because it does not block blood vessels. Growth factors and various factors in PL are essential in wound healing, nerve repair, bone regeneration, angiogenesis, migration, and cell adhesion, and these are the factors that make PL effective. There are several

reasons for the various effects of PL, including the use of different materials, pH changes, the method of preparing PL, and the use of autologous or non-autologous PL. PL for the treatment of diseases such as alopecia, infertility after chemotherapy, wound healing, periodontal defects, oral mucositis (due to PDGF), osteoarthritis (due to increased chondrocyte cell proliferation and mesenchymal stem cells), GVHD (supplement for stem cell proliferation) And transplantation in patients resistant to corticosteroids), in bone regeneration (due to the presence of growth factors, adhesive molecules and cytokines), eye disease (effective in repairing corneal damage, nerve cell regeneration), in therapeutic cells (reducing cell culture time and increasing Cell production) is useful. However, PL may reduce the immunosuppressive effect of mesenchymal stem cells. The presence of fibrinogen in PL may have adverse effects on the modulation of mesenchymal stem cell immunity. High growth factors can cause some side effects such as excessive angiogenesis and corneal fibrosis.

Conclusion: Evidence suggests that HPL has the potential to become a standard product for tissue engineering as well as for regenerative purposes as a pure orthobiologics. While no serious side effects have been reported in the clinical use of HPL, further studies and standardization are still needed to obtain the best version of this advanced cell-free product, and this product should be used with caution. Human platelet lysis can be considered as a suitable alternative to other blood products such as PRP, platelet gel and human serum. However, pathogen inactivation methods (especially virus reduction) may be required, elimination steps to improve the safety of cell therapy products and assess risk with epidemiology. There is also a need to include blood bank rules and standardization of consumables. In general, its preparation should be standardized. Finally, using a set of healthy donors can minimize individual diversity. More research is needed to better understand the performance of PL in other parts of the body, including the femur and various species. It is also suggested that all materials in PL should be properly weighed to determine the impact of each factor for different applications.

Keywords: HPL, Growth factors, platelet, PRP, FBS

Portage and screening for viral hepatitis B in pregnant women in Kabul, Afghanistan (Research Paper)

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Introduction: Background: Viral Hepatitis B remains a major public health problem because of its frequency and the costs involved. Objective: To determine the carriage and compare the different screening methods for hepatitis B infection in our environment

Methods: This is a cross-sectional descriptive study conducted in collaboration with Wazir Akbar Khan, Afghan Japan, Blossem Hospitals in Kabul: Kabul Maternity Hospital, Wazir Akbar Khan General Hospital, Afghan Japan General Hospital and Blossem General Hospital. The centers were selected randomly based on the presence of women in Prenatal Counseling (PNC) and access to the centers. All women who referred to PNC in the centers from June 1 to August 29, 2018, were included in the group after signing an informed consent. Blood samples were collected by the technical team of the centers and transferred to the laboratory for analysis according to the cold chain at 4 Â° C. Each sample was tested for serological research for HBsAg antigen and ELISA sandwich in the medical diagnostic laboratory of Wazir Akbar Khan Hospital.

Results: 212 women agreed with this study. The highest representative age is 30 to 55 years with 75 women (48.6%). 65 women (31.9%) were housewives. 79 women (41.3%) had primary education. 89 women (38.8%) with HBsAg serology were positive for HBV and 106 (50%) were positive for ELISA. The most infected age group was 33 to 55 years (42.1% by RDT and 52.6% by ELISA). More cases of infection were observed among housewives (49.2% by RDT and 63% by ELISA) compared to other occupations. 186 women had not received the hepatitis vaccine (91.2%), of which 38.7% were positive for HBsAg and 51% were positive for ELISA. On the other hand, 26 women (8.8%) received hepatitis vaccine, of which 38.9% were positive for HBsAg and ELISA. 134 women had a history of blood transfusion (65.7%), of which 41% were positive for HBsAg and 56% were positive for ELISA. On the other hand, 70 women (34.3%) had no history of blood transfusion, of which 34.2% were positive for HBsAg and 38.6% were positive for ELISA.

Conclusion: The study shows that hepatitis B does represent a public health problem among pregnant women in the city of Kabul. The seroprevalence of viral hepatitis B in pregnant women remains very high. ELISA appears to be a better technic for the diagnosis of HBV.

Keywords: Viral Hepatitis B, Pregnant women, kabul

Potential value of miR-214 as a diagnostic biomarker and therapeutic target in multiple sclerosis (Research Paper)

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Introduction: Multiple sclerosis (MS) is an autoimmune chronic inflammatory disease of the central nervous system. The T/Treg cells imbalance plays a crucial role in pathogenesis of this disease. The diagnosis of MS primarily based on disease symptoms such as white matter lesions on MRI and there is no specific lab-based test. The differential expression profile of miRNAs in MS patients suggests that they may have key regulatory roles in the development of MS, therefore miRNAs have potential value as a therapeutic/diagnostic target in MS. In this study, miR-214 expression levels, its target genes, and genetic pathways in MS were investigated using bioinformatics databases.

Methods: At first, the complete information for miR-214 gene including its chromosomal location, expression, function, and its related disorders, pathways, orthologs was obtained from miRBase and GeneCards databases. Gene ontologies and MS signaling pathways associations of miR-214 targets were analyzed by DAVID Bioinformatics Resources 6.8.

Results: The gene of human miR-214 is located in the chromosomal region 1q24.3, within intron 14 of the dynamin-3 gene and expressed abundantly in the extracellular space and plasma membrane. The previous studies demonstrated that miR-214 play important role in a variety of cancers. The present study revealed that miR-214 has a significant effect on 3865 identified genes, of which 2534 target genes impress in chronic diseases such as MS. Further analysis demonstrated that miR-214 is associated with 65 genes in MS. It was found that the mTOR signaling pathway is a potential target for miR-214. The inhibition of this pathway by miR-214 results in more expansion of regulatory T cells compared to effector T cells.

Conclusion: The current study shows that, miR-214 plays the crucial role in multiple sclerosis by affecting various genes and signaling pathways. Therefore, miR-214 can be used as a biomarker in early prevention. Furthermore, it has a potential value in the MS treatment via restoration of T/Treg cell balance and it raises hopes for a cure given the challenges ahead.

Keywords: miR-214, multiple sclerosis, diagnostic biomarker, therapeutic target

Protectivity of combination of two outer membrane proteins against Acinetobacter baumannii infection in murine model (Research Paper)

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Introduction: The ability to absorb iron in its absence and to form biofilm has led to the development of multidrug-resistant isolates of Acinetobacter baumannii, making this pathogen a major global concern. Biofilm makes A. baumannii resistant to a wide range of antibiotics and disastrous environmental conditions. Biofilm-related protein (Bap) plays an indispensable role in biofilm formation by this pathogen. Bap is one of the most acidic and largest bacterial proteins with pI of ~3 and 8620 amino acids. Bap-related proteins are engaged in intercellular adhesion in the full-grown biofilms and are located in the outer membrane of Acinetobacter baumannii. On the other hand, the element iron is vital for the colonization and growth of the pathogen in its host. Acinetobactin (the siderophore of Acinetobacter baumannii) in iron deficit conditions gives A. baumannii the ability to absorb adequate iron over an extensive range of pH and Baumannii acinetobactin utilization (BauA), the most important member of the iron-regulated outer membrane proteins (IROMPs), absorbs the acinetobactin-ferric complex and inserts it into the periplasm of this bacterium. accordingly, disruption of BauA and Bap function can prevent the growth and formation of biofilms in the host and cause the elimination of this pathogen. BauA and Bap seem to be the most promising targets for developing a vaccine against Acinetobacter baumannii.

Methods: In this investigation, we expressed BauA and Bap at molecular weights of 78 and 41 kDa in competent cells of E. coli BL21 (DE3) and then purified them. Two purified surface proteins of Acinetobacter baumannii, Bap and BauA, were injected subcutaneously into three groups of BALB/c mice. Mice in the first group received Bap, the second group received BauA, and the third group received both proteins. This was done to induce antibody responses to protein antigens. The survival of mice was then appraised in challenge with heterologous strains of Acinetobacter baumannii.

Results: Bap and BauA were already reported to raise antibodies against these proteins. The same results were obtained. The combination of the two antigens led to significant protection against A.baumannii in comparison to the single antigens.

Conclusion: Administration of combined antigens triggers better protection than single antigens

Keywords: Acinetobacter baumannii., Antigen., Antibody, Vaccine., Bap., BauA

Review of blood substitutes and Future blood transfusion (Review)

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Introduction: The first experimental transition after the incident concerning Pope Innocent VIII, thereof blood flow English health practitioner William Harvey (1578-1657), whom he studied medication in Padua after which labored at St Bartholomewâ€™s the London hospital became the primary to explain this in detail blood flowed via the systemic move of blood vessels in one direction, . By 1907, doctors were mixing small amounts of blood before transfusing blood. If no clots were seen, the blood groups tested were thought to be compatible. This allowed doctors to save thousands of lives and lay the groundwork for modern blood transfusions. Up to this point, all blood transfusions occur at the right time and directly between two people. This is because the blood begins to clot almost immediately after contact with air due to the defense mechanism to prevent excessive bleeding after various injuries . Why can we want blood substitutes? Increasing public bad perceptions approximately blood safety coupled with the potential danger of transmitting diseases, consisting of hepatitis, human immunodeficiency virus and, maximum, particularly in the UK, transmissible spongiform encephalopathies, specifically, bovine spongiform encephalopathy (BSE) 6 and, Perhaps, version Creutzfeldt-Jacob disease (vCJD), have brought about blood shortages and fuelled the improvement of referred to as blood substitutes.

Methods: We found roughly 40 publications in Google Scholar, Scopus, PubMed, and other databases and chose 12 to write our review article. We looked up terms like biotechnology in blood transfusion, artificial blood, and future blood transfusion. Our search constraint was limited to English. Geographical restriction not included. The period 2016-2020 was searched. Review and original articles were reviewed simultaneously.

Results: The maintenance of coagulation factors, the absence of subsequent thrombocytopenia, and the reduction of injected anticoagulants are just a few of the benefits of WB (Whole Blood). The most important impact on transfusion medicine would be the use of recombinant albumin and F VIII, which are already in preclinical or clinical trials. In addition, this technique is also important for the cloning of viral antigens for the development of new or more sensitive

tests for testing viral infections.Using corresponding DNA probes is One of the first and to date, most important areas for the use of is possible to monoclonal antibodies in diagnosis is the determination of leukocyte and lymphocyte subsets e.g. T- and B-cells. The second approach to the development of blood substitutes involves the use of PFC liquids two compounds investigated most are perfluorodecalin, a bicyclic perfluorinated alkane, and bromo perfluoro-n-octane. As a transfusion alternative, phospholipid vesicles or liposomes encapsulating purified and concentrated human hemoglobin have been produced. They're free of blood-type antigens and infectious viruses, and they're stable and long-lasting. HBV's cellular structure protects cells from the negative effects of Hb molecules by preventing direct interaction of Hb with blood components and the endothelium lining. The cellular structure of HBV is critical for controlling interactions with endothelium-derived vasorelaxation factors, according to microcirculatory findings. The ability of HBV to transport oxygen is demonstrated in animal investigations of extensive hemodilution and resuscitation from hemorrhagic shock. HBVs are finally trapped in the reticuloendothelial system and destroyed, according to biodistribution and metabolism studies.

Conclusion: These artificial blood replacements offer the advantages of not requiring compatibility testing, being free of blood-borne pathogens, having a long shelf life, and not requiring refrigeration. Newer possibilities of therapeutic application of blood substitutes in clinical practice are emerging, ranging from fetal hypoxia in preeclampsia, cerebral ischemia, and liver transplantation, to contrast agents or infection tracers, according to recent literature. Future research efforts in this area should focus on the fact that current blood substitutes lack the immunologic and coagulation qualities that are important to human blood. Artificial blood is expected to have a significant impact on the future development of medical care, so efforts should be focused on developing adequate quantities of safe, effective, commercially viable alternatives with fewer drawbacks that will reduce reliance on donated blood and reduce mortality from transfusion-related complications. As a result, a new avenue in the field of transfusion medicine opens up a world of possibilities. It will be fascinating to see if a completely functional human Hb can be created and retrieved intact from plant systems in the future.

Keywords: Blood transfusion,, blood substitutes,, perfluorodecarin,,

Review of cartilage regeneration through injectable microgels (Review)

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Introduction: One of the tissues in the body that is faced with regeneration difficulties is cartilage [1-7]. Common approaches used for treating cartilage abnormalities are stem cell injection and cartilage tissue engineering. Stem cell injections result in poor cell survival, whereas cartilage tissue engineering leaves a large wound and fails to fill uneven flaws after implantation. However, because of their customizable structure and capacity to accommodate bioactive substances, and their ability to be locally supplied to fill irregular defects, injectable hydrogels have been employed for cartilage regeneration [1, 7]. Natural materials such as collagen, alginate, hyaluronic acid, chitosan, and gelatin or synthetic materials such as polyethylene glycol can be utilized to make hydrogels [5]. Microfluidic technology and photopolymerization processes are used to create microgels, which are growth factor-loaded methacrylated hyaluronic acid and heparin blend MGs that can recruit endogenous mesenchymal stem cells and promote chondrogenic differentiation [8]. Microfluidic microgel is an appropriate cell carrier for preventing injection-induced shear stress damage to encapsulated stem cells [5, 8]. As a result, we believe that the microgel-based strategy that has emerged as one of the most promising types of cartilage regeneration has a bright future in novel methods of articular cartilage repair.

Methods: We used PubMed, Medline, Google scholar, science direct, and Embassy databases to conduct a systematic literature search using cartilage, Mesenchyme stem cell, Biologist, PRP, ACI as keywords in our search terms. We considered a language limitation as English and a time limit for 2019-2022 due to the increase and advances made in the subject in this period. The criteria for including studies in our review encompassed clinical studies on ASC injection conducted on humans for cartilage regeneration. We screened 320 articles using the PRISMA checklist to exclude duplicates and improper studies. We discovered clinical investigations on ASC therapies for cartilage abnormalities in 17 articles. Also, a scoping evaluation of the existing scientific literature for hip biologics was conducted, with evidence for hyaluronic acid

available (HA), platelet-rich plasma (PRP), stem/stromal cells, microfracture, mosaicplasty, osteochondral allograft, and cell-based therapies investigated.

Results: As mentioned, there are several different methods for engineering cartilage, and each has its advantages and disadvantages. Since articular cartilage is engaged in weight-bearing and has a relatively low intrinsic healing potential, there are various barriers to regenerative therapies [9]. As a result, it is critical to employ proper tissue engineering materials and cell types in cartilage regeneration [9]. There are two possible prevention techniques for hyaline cartilage fibrosis: 1) Reshape the injury's microenvironment. 2) Increase the migration of endogenous skeletal or mesenchymal stem cells to the articular cartilage [6]. The response of endogenous cells is one of the sources of cell-laden microgel. In addition to the influence on encapsulated cell types, the microgels may affect endogenous cells, which substantially impacts the entire healing process [7]. Three main strategies used for tissue-engineering articular cartilage are: 1) Cell-scaffold construct. 2) Scaffold-free 3) Cell-free. The last method utilizes endogenous stem cells indirectly [4]. The scaffold-based strategy has limitations, including unavailable cell sources, morbidity at the donor location, and chondrocyte phenotypic instability in culture [10]. The risks of morbidity associated with arthroplasty are significant. Another challenge of surgery is the painful repercussions and short lifespan of implanted prostheses [11] [12].

Conclusion: Mesenchymal stem cell-based therapies offer a great way to revolutionize the treatment of cartilage defects, and it has been shown that the mechanisms of mesenchymal stem cell cartilage regeneration are related to nutritional factors and direct grafting. Exosomes are very important as extracellular vesicles among nutritional factors [12] [9]. There are several difficulties related to isolating and growing, differentiating, and preparing mesenchymal stem cells for placement in degenerated joints, and it can be dangerous if these cells are exposed to abnormal physical loads on anatomical structures. Therefore, future reconstructive medical strategies must address these remaining concerns [9]. More investigations need to be done into this area. Better-designed studies are required to elucidate the precise mechanism of action of the treatment and the general application of these stem cells to treat OA with cartilage regeneration. [12].

Keywords: Cartilage regeneration, Cell-laden injectable microgels, Articular repair, Challenges for Cartilage

Review of properties of metal nanoparticles in antibiotic resistance (Review)

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Introduction: Antibiotic resistance in microbes Due to the recent outbreak of microbial resistance, it is becoming increasingly important in public health care. The global is transferring toward the post-antibiotic era.Excessive and uncontrolled use of antibiotics, both in preventive and curative health care, has exacerbated the situation because microbes that have never been exposed to antibiotics, due to the transfer of gene encoding, resist that drug [1]. Research is now focused on finding solutions to this problem by creating nano-antibiotics and increasing the performance of existing antibiotics [2].

Methods: The keywords Nano-antibiotic, Metal nanoparticles, Antimicrobial activity were searched in pubmed and google scholar databases between 2015 and 2022.

Results: Metal nanoparticles interact with cellular components and biomacromolecules, including DNA and RNA, to alter cellular processes. In terms of antimicrobial activity, metal nanoparticles at nanomolar concentrations show excellent results in inhibiting bacterial strains [3]. Silver nanoparticles are the most common disinfectants. Silver is particularly good as an antibacterial agent because it crosses bacterial cell walls and can be absorbed by bacterial cells [4]. Nanoscale CuO reduction provides high levels and reactivity to interact with bacteria. CuO nanoparticles cause oxidative stress and the production of reactive oxygen species, which are lethal to pathogens. The synergistic combination of antibiotics and CuO nanoparticles significantly reduces the biofilm in various ways. A drug like amoxiclav is lethal by inhibiting the cell wall biosynthesis of bacteria. When used in a synergistic combination, CuO nanoparticles may bind to beta-lactamase, rendering it ineffective for cleavage of the beta-lactam ring [5]. ZnO nanoparticles (ZnO) have been tested in vitro against clinical isolates of MRSA and MSSA, but are more effective than copper or silver nanoparticles because they cause cell lysis by damaging lipids and proteins in the bacterial cell membrane, resulting in Leakage of cytosolic materials [4]. AuNPs are promising bactericidal agents due to their versatile optical and photothermal properties. Although not as well studied as the antibacterial mechanism of AgNPs, the antibacterial activity of AuNPs is believed. AuNPs inhibit cellular metabolism by altering membrane potential and inhibiting ATPase activity, and by binding to the ribosome subunit to inhibit tRNA binding, leading to disruption of biological processes [6].

Conclusion: According to previous studies, antibacterial activity in nanomaterials is due to the observed biophysical interactions between nanoparticles and bacteria, including cell adsorption and accumulation of nanoparticles, which leads to membrane damage. In particular, metal

nanomaterials (such as silver, copper, zinc, and gold) exhibit desirable physicochemical properties that lead to significant levels of antibacterial activity. This study focuses on recent advances in metallic nanomaterials of silver, copper, zinc and gold as antibacterial agents with a focus on antibacterial activity [6]. Currently, the field of nano-antibiotics is hardly in its infancy compared to targeted nanomedicine for the treatment of cancer and cardiovascular disease, and there is very little information about the clinical applications, toxicity, and antibacterial mechanisms of nano-antibiotics [7].

Keywords: Antibiotic resistance, Nano-antibiotic, Metal nanoparticles, Antimicrobial activity

rs372321755 as a new deleterious single nucleotide polymorphism related to NOD2 gene in inflammatory bowel disease (Research Paper)

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Introduction: Introduction: Inflammatory bowel diseases (IBD) is a complex and multifactorial condition characterized by chronic gastrointestinal tract inflammation disease. Types of IBD include Crohn's disease (CD) and ulcerative colitis (UC) [1]. Crohn's disease is manifested as patchy transmural inflammatory patterns that affect all layers of the intestinal wall in any portion of the gastrointestinal tract, whereas ulcerative colitis is limited to the innermost layers of the mucosa in the large intestine. CD and UC mainly affect young people, causing bloody diarrhea, abdominal pain, malabsorption, fatigue. Long-lasting inflammation also increases the risk of colorectal cancer in patients with IBD and thus, affects the quality of life of patients [2]. Different studies indicated that NOD2 gene is associated with IBD. The NOD2 protein is active in several types of epithelial cells, including Paneth cells, which are found in the lining of the intestine. These cells help defend the intestinal wall against bacterial infection [3]. Single nucleotide polymorphisms (SNPs) are a type of polymorphism involving variation of a single base pair [4] and when arising in genes can impact on their expression. Therefore, identification and studying the correlation of SNPs with diseases is important for understanding the pathology of them. Also, the SNPs that are associated with target genes may be used as biological markers for prognosis of diseases. Thus, this study carried out to identify the possible new deleterious SNPs in IBD.

Methods: Methods: Online bioinformatics tools, including NCBI, PROVEAN, SIFT and HOPE, were used for the identification of SNPs associated with NOD2 gene and also for the evaluation of their effects on the protein that is coded by this gene.

Results: Results: In the present study, various SNPs extracted in the coding region of NOD2 gene. In this regard, the results of SIFT and PROVEAN revealed that rs372321755 is the most significant deleterious SNP in the protein-coding region of NOD2 gene. It also found that rs372321755 induced the substitution of the wild-type A allele with the mutant-type G allele in the NOD2 gene. Moreover, HOPE results indicated that this SNP is cause the Methionine mutation into Valine at the 28nd position of NOD2 protein that this mutation is probably damaging to the protein. In this regard, the wild-type and mutant amino acids differ in size. The mutant residue is smaller, this might lead to loss of interactions.

Conclusion: Conclusion: This study introduces rs372321755 as a new dangerous SNP that is associated with NOD2 gene and inflammatory bowel

disease. The occurrence of this point mutation in NOD2 gene a gene may increase the incidence of IBC by altering the structure of the NOD2 protein.

Keywords: Keywords: NOD2 gene, Single nucleotide polymorphisms, In silico analysis, rs372321755, Inflammatory

Scfv of Nimotuzumab can enter EGFR-overexpressing cancer cells (Research Paper)

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Introduction: Introduction The epidermal growth factor receptor (EGFR) is a glycoprotein tyrosine kinase receptor which is the main factor in controlling of the cell growth and viability. Since this receptor is overexpressed in many carcinomas, it is regarded as an ideal target for cancer therapy and imaging. Anti-EGFR monoclonal antibodies can be engaged to specifically deliver small molecules with therapeutic or diagnostic properties to EGFR-overexpressing cancer cells. Therefore, in the current study, we evaluated the ability of single-chain Nimotuzumab molecules in recognizing and entering EGFR-overexpressing cancer cells.

Methods: Methods Amino acid sequence of Nimotuzumab variable domains (VH and VL) was obtained from the protein data bank (PDB). Nine arginine residues (called 9-R) was added to N-terminus of VH domain to form a scFv in VH-linker-VL format. After gene synthesis and cloning into pET22b (+), the recombinant was expressed and conjugated to FITC. The conjugate was tested on A-431 (EGFR-overexpressed cells) and MCF-7 (EGFR low-expressed cells) cancer cells. Scfv molecules lacking 9R segment was used as a control.

Results: Results Both the molecules were found to enter the cancer cells (A431 Cells) in an efficient manner and emit signals. No obvious difference was found between CPP-containing and CPP-lacking molecules in entering cancer cells.

Conclusion: Conclusion 9R-nimotuzumab ScFv is able to recognize and enter the EGFR-overexpressing cancer cells. CPP is not an essential component for cellular internalization.

Keywords: EGFR, 9R-scFv, scFv, A-431, MCF-7.

Selection of appropriate scaffolding in the process of spinal cord injury repair (Review)

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Introduction: Spinal cord injury is associated with inflammation and destruction of neurons and glial cells ØŒ With a mortality rate and disability of 25,000 to 50,000 people The gradual destruction of the tissue around the primary trauma, known as secondary injury, also limits treatment. The cell therapy strategy is appropriate along with the selection of the scaffold The scaffold has biodegradable and biocompatible properties and also facilitates cell cohesion In addition, the cell environment, while controlling physical and biochemical stimuli, coordinates cellular processes, including proliferation, differentiation, movement, and apoptosis. Therefore, a successful scaffold requires the creation of a suitable environment for cell life and its proper functioning on a small scale, and this is the direct role of the environment in which not only the cells are located, but also determines its type. Cellular behavior The types of biomaterials used, A) Have a natural origin such as collagen, alginate, chitosan, fibrin, and hyaluronic acid B) Synthetic origin: such as polyglycolic acid, polylactic acid, and their co-polymers C) Ceramics include calcium phosphate and bioglass d) metals such as magnesium, titanium, and selenium. Scaffolding fabrication and shaping methods also include freeze-drying, electrospinning, solvent casting, gas foam, melt molding.

Methods: This study is a review of articles from 2009 to 2021 Articles were selected from Science Direct and Scopus

Results: Nanofibers support nerve regeneration, and their porous networks are very similar to the extracellular matrix. Also, spatial orientation and its structural type cause cell proliferation and differentiation Due to the use of cells, the challenge is to choose the right polymer as well as the optimal scaffold production method that is mechanically suitable. On the other hand, spatial orientation and scaffold configuration type are effective in the slope of cell growth and proliferation.

Conclusion: Development and selection of scaffolding has an effective role in nerve repair Therefore, it can be said that many scaffolds are able to cause cell adhesion but have little support for the damaged part. Natural polymers show more support. On the other hand, nanofibers are a more suitable tool for the treatment of spinal cord injury.

Keywords: Nanofibers- spinal cord injury- Biomaterial-Electrospinning

Soluble expression of human recombinant interleukin 11 in SHuffle T7 E. coli using pET system (Research Paper)

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Introduction: Human interleukin-11 (hIL-11) is a cytokine that has multiple physiological properties involving hematologic, immunomodulatory, and epithelial effects. Recombinant hIL-11 has been shown to increase the platelet counts in animals and human. It is the only drug approved for use in chemotherapy-induced thrombocytopenia (CIT). The recombinant form of the cytokine differs from the native protein by of a proline residue at the amino terminus, resulting in a 177-amino acid protein. Oprelvekin is the drug form of recombinant hIL-11 that stimulates megakaryocytopoiesis and thrombopoiesis. In studies of mice and nonhuman primate with moderate and severe myelosuppression or compromised hematopoiesis, oprelvekin was shown to potently induce thrombopoiesis, improve platelet nadirs and accelerate platelet recoveries compared to the control groups. The drug has other important effects such as regulates intestinal epithelium growth, inhibiting adipogenesis, suppressing the pro-inflammatory cytokines release by macrophages, and inducing acute-phase protein synthesis. In the present study, the coding sequence of hIL-11 with His-tag in its upstream was inserted into pET15b/Trx that contained an independent cassette for expression of thioredoxin. The aim of the construction of recombinant plasmid (pET15b/Trx/hIL-11) was to simultaneously but separately express of recombinant hIL-11 along with thioredoxin as a solubilizing tag. The co-expression of thioredoxin was accomplished to improve the production of the soluble and active form of recombinant hIL-11 in SHuffle T7 E. coli as the host cell with enhanced capacity to correctly fold protein with multiple disulfide bonds. Meanwhile, with separate co-expression of hIL-11 with thioredoxin, it is no need to digest the expressed protein and isolate the solubilizing tag from the recombinant cytokine.

Methods: In this study, the CDS of human IL-11 with a His-tag in the structure of pGH plasmid was digested with appropriate restriction enzymes and was sub-cloned into pET15b contained the a separate expression cassette of thioredoxin (pET15b/Trx/hIL-11). Finally, the plasmid was transformed into SHuffle bacteria, which were cultured in LB broth medium containing ampicillin. The positive colonies that contained pET15b/Trx/hIL-11 were selected. Successful expression of the soluble recombinant hIL-11 protein in bacterial cells was achieved using IPTG induction when the OD600 was approximately 0.6.

Results: Induction of recombinant protein production was performed using 0.1 mM IPTG at 30 Â°C for 6 h. After this time period, the cells were harvested and lysed with cell lytic solution. Total protein was extracted and the expression of the recombinant protein was evaluated using 15% sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE). Eventually, the recombinant hIL-11 protein was purified with Ni-affinity resin and analyzed again with 15% SDS-PAGE.

Conclusion: In the present study, a new subspecies of Shuffle E. coli was obtained by transformation of an expression plasmid, pET15b/Trx/hIL-11, which was efficiently produced the soluble recombinant hIL-11. Production of the soluble recombinant cytokine was verified through SDS-PAGE analysis. Moreover, the efficient purification of recombinant hIL-11 with Ni-affinity agarose was confirmed by SDS-PAGE in which a protein band was observed with the size of about 24 kDa in comparison to the negative control contained a sample of the extracted protein from the E. coli cells harboring intact pET15b plasmid.

Keywords: Human Interleukin 11,Recombinant protein, Soluble expression , pET system

Stem Cell-based Therapies as a Promising Approach in Alzheimer's Disease (Review)

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Introduction: Alzheimer's disease (AD) is a progressive neurodegenerative disease and is the most common cause of dementia in the elderly population. In this disease, the process of neurodegeneration begins with the formation of amyloid plaques in the brain, and progressive neuronal cell death leads to cognitive disorders and memory loss in the patients. AD is currently incurable and present treatment options only reduce the symptoms in patients and cannot prevent neurodegeneration. So far, many attempts have been made to develop small therapeutic molecules or antibodies to treat AD, but they were mostly inconclusive. To date, stem cell-based therapies have become a promising new approach for regeneration process in neurodegenerative disorders, including AD. Stem cells are undifferentiated cells which have the ability to proliferate, self-renewal, and differentiate into different cell types, including neurons. For this reason, they can be used in the production of various cell types and tissues engineering. Successful results in the production, proliferation and differentiation of stem cells in animal models of AD indicate the therapeutic potential of stem cells in the treatment of neurodegenerative disorders. Accordingly, stem cell therapy may provide an opportunity to treat or delay the progression of AD.

Methods: This review performed by searching "Alzheimer's disease" AND "Stem Cell Therapy" AND "Regenerative Medicine" keywords (Title/Abstract) in PubMed, Scopus, Embase, Google Scholar, and Web of Science databases. All original articles (human and animal) written in English were included in this study.

Results: In recent years, the use of stem cells derived from various sources in preclinical studies has been effective in controlling and treating symptoms in animal models of AD, and clinical trials are currently underway in humans. Mesenchymal stem cells (MSCs), induced pluripotent stem cells (iPSCs), embryonic stem cells (ESCs), and neural stem cells (NSCs) are the most common type of stem cells used in the studies for AD which are mainly transplanted intravenously into the body. MSCs have easy isolation and handling without ethical restrictions. These cells were able to cross the Blood-Brain Barrier (BBB) and migrate to damaged areas of the brain. The results of transplantation of MSCs into AD animal models showed the potential for neuroprotection by modulating neuroinflammation, increasing neurogenesis, and suppressing neuroapoptosis. Therefore, they can be used clinically in patients with AD. IPSCs are pluripotent stem cells which reprogrammed in vitro from adult somatic cells and can differentiate into different cell types, including neurons. Despite their promising applications in AD animal models, these cells are ethically controversial, and have many concerns about genetic mutations in

the process of iPSCs generation, tumorigenicity, teratoma formation, and immunogenicity. Therefore, the applications of iPSCs in AD have so far focused more on the development of disease models than on treatment. ESCs are obtained from the inner cell mass of blastocyst. They can be the best cellular source for cell therapy studies if pluripotency can be controlled to desired phenotype. Despite the good results obtained in preclinical studies on AD models, duo to the possibility of teratoma formation, tumorigenicity, poor survival rate after transplantation, and ethical limitations, the studies on these cells has been limited in clinical trials compared to other stem cells. NSCs are present in different areas of the adult central nervous system and are able to differentiate into different cell types, including neurons, oligodendrocytes, and astrocytes. NSCs can also be differentiated from brain tissue of aborted fetal, iPSCs, and ESCs. In animal models of AD, transplanted NSCs were able to differentiate into mature brain cells and improved the brain function and cognitive abilities of mice. NSCs showed lower risks in tumorigenicity and immunogenicity which makes them the potential candidates for neural transplantation in human. However, their ability to generate specific neurons remains unknown, and unwanted differentiation into non-neuronal cells, like glia, has been reported.

Conclusion: The successful results of many preclinical studies indicate the ability of stem cells to treat animal models of AD. However, stem cell-based therapies for AD in clinical trials are in its early stages and more evidences are needed to support its effectiveness and safety for human studies. Along with their countless benefits, ethical concerns, reprogramming efficiency, tumorigenicity, immunogenicity, and the risk of uncontrolled proliferation and differentiation after transplantation should also be considered before use in a wide range of patients.

Keywords: Neurodegenerative diseases, Alzheimer's disease, Regenerative Medicine, Stem cell Therapy

Stem cells and their role in the treatment of diabetes (insulin production) (Review)

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Introduction: Diabetes is the most common endocrine disease. The lifelong need for frequent blood sugar monitoring, insulin injections, and dietary restrictions are highly undesirable and annoying for diabetic patients. On the other hand, treating the complications of diabetes imposes a lot of financial burden on society. In the last decade, pancreatic islet transplantation has been widely considered a potential treatment for diabetes. This has always been difficult due to restrictions on the purification of islands from the corpse. Stem cells are renewable cellular sources that serve as an alternative to organ or tissue transplantation. The possibility of using stem cells in the treatment of diabetes and the production of insulin-producing islets has long been of special interest to scientists in various scientific centers and is almost one of the hopes for the future control of diabetes. In animal studies, human stem cells derived from hematopoietic organs, liver, pancreas, and human embryonic stem cells are some of these cases. This article reviews the course of studies conducted in this regard.Approximately 5â€“10% of all diabetic individuals suffer from type 1 diabetes. Recent studies have emphasized the importance of strict glycemic control in order to reduce ophthalmologic, neurological, and renal complications of the disease. The need to use a method that can replace the lost insulin-producing cells in type 1 diabetes and thus completely cure type 1 diabetes has led scientists to use stem cells in this field. These cells have the unique property that they can potentially become any of the adult cells in the body. Stem cells can be isolated from human embryos or even adults. Theoretically, embryonic stem cells can be cultured outside the body and transform into insulin-producing cells using a variety of methods, including the use of â€œgrowth factors,â€• and when sufficient amounts of these cells are available. They can be used to treat any diabetic person who needs these cells. These cells can also be genetically engineered to resist the recipient's immune system and transplant rejection, which is not possible with adult stem cells. It is also possible to place these cells in a non-immunogenic agent to prevent them from being rejected by the immune system and to eliminate the need for anti-transplant drugs. An interesting recent study on stem cells in adults showed that if stem cells in the walls of pancreatic ducts in adults were cultured in the laboratory, they could be stimulated to form a true cell mass. Not only is it able to secrete insulin, but it is also able to increase or decrease the amount of secretion based on the blood sugar of the environment, which is essential for the success of the transplant. However, the most important concern about stem cell transplantation is the risk of developing cancerous tumors in the recipient, especially when embryonic stem cells are used.

Methods: In this review study, databases include pub med, Springer, Google Scholar, and Science direct, SID, American diabetes association; and keywords like Treatment of diabetes, stem cells, Insulin production, were used

for collecting the articles. I reviewed all articles since 2001 and removed those that were not relevant to the study domain from the study process.

Results: Studies in animal models have shown that the grafting of stem or pluripotent stem cells can successfully cure many of our diseases, including diabetes

Conclusion: Although the theory of using stem cells, especially embryonic cells, for the definitive treatment of diabetes and providing an ideal treatment is very interesting, and some animal experiments are promising, after two decades of research, according to what has been said, still is not possible to use it as a common treatment for diabetes. There are still many problems and questions on the way to the ultimate goal that scientists must answer with numerous animal and laboratory experiments to re-enter the human experience and eventually, if successful, to be used as a treatment, so This method has been kept at the research level.

Keywords: Stem cells _ Treatment of diabetes _ Type 1 diabetes _ Insulin production

Stop angiogenesis using plant nanoemulsions (Review)

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Introduction: Angiogenesis plays an important role in physiological (embryogenesis) and pathological conditions (some diseases, including cancer). Nanotechnology in the last decade has had a wide impact on various areas of human life, including pharmacy and medicine. In recent years, much attention has been paid to the preparation of polymer nanoparticles as drug carriers because nanoparticles can be used as a drug delivery system due to controlling and slowing down drug release, smaller particle size than the cell, biocompatibility and increasing therapeutic efficacy of the drug. To be considered very effective.

Methods: Encapsulation of anti-angiogenic compounds and their use to seal the angiogenic process in the fight against various diseases has been considered by many researchers. Therefore, in many studies, silver nanoparticles are used to reduce the process of angiogenesis, but in principle, these structures are unpredictable due to their chemical composition, lipophilic properties, catalytic activity, etc. Nanoparticle structures, despite their very small size, over time may lead to leukocyte poisoning by entering these cells, as well as indirect damage to DNA and more. Therefore, plant nanoemulsions should be used to better control angiogenesis.

Results: Black cumin extract is one of the most widely used extracts, which includes cumin aldehyde, paracetamol, alpha-phenine and gamma-terpene, which are often terpene compounds that have biological effects in the pharmaceutical and food industries. Also, vegetable oils are a good candidate for the treatment of some diseases, including cancer, due to their phenolic compounds.

Conclusion: Studies have shown that nanoemulsions synthesized from plants have toxic effects on the cell, which leads to inhibition of cell proliferation and ultimately leads to the cessation of angiogenesis, mimic angiogenesis.

Keywords: Angiogenesis,, nanoparticles, plant emulsions,,cumin, tomur

Synthesis and Characterization of Artemisinin-Chitosan/Alginate Nanoparticles as a Drug delivery System for Prostate Cancer Treatment (Research Paper)

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Introduction: Background: Prostate cancer remains as the most frequently diagnosed malignancy in men worldwide. Conventional treatments such as radiation therapy and chemotherapy are undesirable due to the adverse effects on healthy cells and drug resistance. Artemisinin, a natural compound derived from Artemisia annua, also known as sweet wormwood, is an effective anti-malaria agent that has recently been found to have anti-cancer effects on prostate cancer. However, its poor water solubility, low bioavailability, and short half-life are the main drawbacks for its use in the clinic. Objective: This study was aimed to fabricate chitosan/alginate nanoparticles as a biocompatible, hydrophilic and low toxic drug delivery system to improve the therapeutic efficiency of artemisinin.

Methods: Methods: Artemisinin-loaded nanoparticles were prepared by ionotropic gelation procedure. The encapsulation efficiency of chitosan/alginate loaded with artemisinin was determined by spectrophotometric assays. Dynamic light scattering (DLS(, Fourier Transform-Infra Red spectroscopy (FTIR), and Field Emission Scanning Electron Microscopy (FE-SEM) techniques were used to characterize the nanoparticles in terms of structure, size, zeta potential, hydrodynamic diameter and morphology. Release profile of artemisinin from the was studied at pH 5.5, and 7.4.

Results: Results: The results showed the encapsulation efficiency and of 61%. The nanoparticles average size obtained from FE-SEM ranged from 30-40 nm with a spherical shape that was optimum for drug delivery. DLS results indicated that zeta potential and hydrodynamic diameter were -45.7 mv and 293.5 nm, respectively. FTIR analysis confirmed the interaction of artemisinin with chitosan/alginate nanoparticles. Drug release indicated an initial fast release followed by a sustained release of 48.30% and 54.71% at pH 5.5 and pH 7.5 after 48 h, respectively.

Conclusion: Conclusion: It could be concluded that Cs/Alg NPs would be a potential carrier of ART for the treatment of prostate cancer.

Keywords: Artemisinin, Prostate Cancer, Nanoparticles, Chitosan/Alginate

Temur therapy with plant secondary metabolites (Review)

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Introduction: Angiogenesis occurs both in physiological conditions (wound healing, embryonic development, etc.) and in pathological conditions (diseases including cancer). This process plays a key role in the growth and invasion of cancerous tissue. Plants are rich in a variety of secondary metabolites used in the food, pharmaceutical and chemical industries. Among these plants, we can mention Barijeh and Choyl. The metabolites of these plants affect the release of MMP_2 and finally the expression of VEGF-e gene is reduced, which stops or reduces the angiogenesis process and the size of the tumor itself. However, some of these metabolites are sometimes produced in limited quantities in plants with special properties, such as anti-melanogenesis and antioxidants in saffron. Crocin and picrocrosins are effective substances in stopping angiogenesis that are found in small amounts in saffron plant, so this restriction can be removed by using plant metabolite engineering.

Methods: Genetic manipulations can be applied to increase the production efficiency of the desired secondary metabolite from a plant, but genetic manipulations are not a suitable system to achieve our goals due to complex and time-consuming processes that often lead to unforeseen results. . Hence gene transfer systems are used. In this article, an overview of Tobacco H. potivirus has been used to transfer the desired gene due to its biosynthetic enzymes and regulatory factors for plants. The recombinant virus is expressed as it enters the plant and the levels of safranal, crocin and picrocrocin in the plant increase.

Results: In N. benthamiana due to the optimal conditions of the plant as a biological plant. By increasing the proper temperature, picrocrosin becomes the inactive structure of picrocrosin, ie safranal, which is very effective in anti-angiogenic activity.

Conclusion: The contents of crocin, picrocrocin increased in fruits and tissues of N. benthamiana treated compared to C. sativus stigma or gardenia SSP. Therefore, to reduce the size of the tumor, the access of this invasive structure from oxygen and .... can be reduced by preventing angiogenesis. The use of plant secondary metabolites as recombinant drugs is a very effective and harmless method in the treatment of many diseases.

Keywords: Safranal, secondary metabolites, virus, gene transfer, tobacco

Test bacterial inclusion body for activity prior to start denaturing and refolding processes to obtain active eukaryotic proteins (Research Paper)

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Introduction: One of a major drawbacks correlated with expressing antibody fragments in bacterial cells is insolubility, which is often regarded as an obstacle in obtaining active molecules. Recombinant proteins aggregated as inclusion bodies within bacterial cells are thought to be unfolded or misfolded, and therefore inactive. So, denaturing and refolding strategies, which are laborious and sometime inefficient, are used to obtain correctly-folded active proteins. In the current study, we show that large quantities of correctly folded and completely active scFv molecules are there in bacterial inclusion bodies; they only need to be isolated from inclusion bodies.

Methods: Method One of a major drawbacks correlated with expressing antibody fragments in bacterial cells is insolubility, which is often regarded as an obstacle in obtaining active molecules. Recombinant proteins aggregated as inclusion bodies within bacterial cells are thought to be unfolded or misfolded, and therefore inactive. So, denaturing and refolding strategies, which are laborious and sometime inefficient, are used to obtain correctly-folded active proteins. In the current study, we show that large quantities of correctly folded and completely active scFv molecules are there in bacterial inclusion bodies; they only need to be isolated from inclusion bodies.

Results: Result The gene encoding 9R-nimotuzumab scFv was synthesized and subcloned into a pET22b(+) vector. The recombinant plasmid was transformed into E. coli BL21(DE3) and the fusion protein overexpressed in bacterial cells under IPTG induction. After lysing cells,, the pellet which contained inclusion body was dissolved in Tris solution without denaturation agents. The recovered protein was evaluated with ELISA assay.

Conclusion: Conclusion ScFv molecules expressed in bacterial cells as inclusion body may be correctly folded and therefore be active. It is better to solubilize inclusion bodies with a non-denaturing buffer and evaluate the activity of recovered protein prior to starting time-consuming, and sometimes inefficient, denaturing and refolding protocols.

Keywords: ScFv, Inclusion body, Native 3D structure, Refolding, Non-denaturing condition

The association between increased expression of PRDX4 and MRPS23 genes with BMI, sex and stage of disease in colorectal cancer (CRC) (Research Paper)

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Introduction: CRC is currently the third leading cause of cancer-related deaths and its incidence is increasing. According to studies, BMI and gender of patients can be mentioned as effective factors in the incidence of CRC .In this study, the genes with increased expression in CRC and its relationship with gender and BMI of patients as well as the stage of the disease were identified.

Methods: CRC risk factors were studied through PubMed and Google Scholar databases and BMI and gender were considered as factors in this study. The Cancer Genome Atlas Program (TCGA) data were used to identify the altered genes expressed in CRC and their relationship with BMI and disease stage as well as the gender of patients. For this purpose, Oncodb database was used and gene expression was normalized by TPM method. At first, the genes that were more expressed in cancer samples compared to normal samples were identified. Common genes between the three factors, (BMI, stage and gender) were obtained using the Interactivenn site. Also, BMI above 29.9 were considered as samples of obese people, between 25 and 29.9 as overweight people, between 25 and 18.5 as normal people and less than 18.5 as underweight people. It should be noted that data classification and review was done with EXCEL 2019 software.

Results: The difference in expression between cancerous and normal samples showed that 1421 genes had significant increase (| logFC |> 1, p-value <= 0.05). Also, the results of the study of the relationship between the expression of these genes with BMI, patients 'sex and disease stage, showed that PRDX4 gene expression with BMI (ANOVA-pvalue = 2.7e-03), patients' sex (ANOVA-pvalue = 4.9e-02) And disease stage (ANOVA-pvalue = 2.6e-03) were significantly correlated. MRPS23 gene expression was also significantly associated with BMI (ANOVA-pvalue = 3.9e-02), patient gender (ANOVA-pvalue = 3.3e-02) and disease stage (ANOVA-pvalue = 2.6e- 02). . PRDX4 gene expression was higher in men and obese individuals as well as patients in stage 1 disease than other groups. Also, the expression of MRPS23 gene was higher in men and obese individuals and patients in stage 2 of the disease than other groups.

Conclusion: The results showed that the expression of PRDX4 and MRPS23 genes increased in CRC and this increase was higher in men and obese

individuals than other groups. Since PRDX4 gene expression was higher in stage 1 disease, this gene is involved in the onset of the disease and can be a good candidate in the treatment of men with CRC with a BMI greater than 29.9 who are in the early stages of the disease. MRPS23 gene expression was also higher in stage 2 of the disease than others. As a result, this gene can be a good candidate in the treatment of men with CRC with a BMI above 29.9 who are in the early stages and stage 2 of the disease.

Keywords: Gene expression, The Cancer Genome Atlas(TCGA), Colorectal cancer (CRC), Oncogene, BMI

The Effect of Catechin Encapsulated Chitosan/Alginate Nanoparticles on Memory Impairment (Research Paper)

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Introduction: Numerous evidence indicated the role of green tea from a traditional beverage to a source of bioactive substances with many health benefits. Green tea is rich in catechin, which mentioned as a polyphenolic compound with favorable properties such as antioxidant, neuroprotective, antitumor, antidiabetic and more others. Albait, catechin promotes the intelligence, memory and strength of the senses, but it removed from circulatory system, rapidly and also it isnâ€™t good enough to act as a therapeutic agent for targeted drug delivery and controlled release in reaching to central nervous system. Due to the unique pharmacology of the catechin, current study designed as a mean of enhancing effectiveness of the catechin at the biochemical and behavioral levels against Aluminum chloride induced Alzheimerâ€™s disease in rat model.

Methods: : Ionotropic gelation method as a non-toxic, simple and controllable method was used for synthesis of the chitosan-alginate nanocarriers containing drug catechin. Physio-chemical characterization of the nanoparticles (NPs) has been detected and approved. Sixty male Wistar rats were divided into six groups (one control group and five treatment groups). In order to evaluated the efficacy and protective effect of catechin loaded NPs (10 mg/kg) and catechin (50 mg/kg) against brain injury caused by AlCl3, the spatial memory impairment model was induced by daily injection of AlCl3 (100 mg/kg) intraperitoneally for 21 days. Afterwards, spatial memory and cognitive function were assessed through Morris water maze task. Also, enzymatic assay of acetylcholinesterase (AchE) catalase (CAT) and total antioxidant capacity (TAC) was performed using hippocampal tissue.

Results: The results indicated that synthesized NPs had optimal physio-chemical characteristics. AChE activity increased in AlCl3 treated group that confirmed memory impairment ($p<0.001$). In contrast, improved memory function was seen through the stability of AchE, CAT and TAC levels in the protective groups that received free and encapsulated catechin. Moreover, based on our findings, the gradual improvement of the learning process in the Morris water maze task and the increase in time spent in the target quadrant on probe day was a confirmation of the effective performance of catechin in the protective groups. However, the AlCl3 receiving group showed a statistically significant correlation with increasing the scape latency and decreasing the time

spent in the target quadrant compared to the control group and other groups ($p<0.05$).

Conclusion: Present study demonstrated that chitosan-alginate NPs elevated the drug catechin performance and improved the memory function. Hence, this therapeutic approach can be applied effectively and propose new aspects for further researches on dementia paradigms.

Keywords: Alzheimer's disease, Catechin, Drug delivery, Chitosan, Alginate

the effect of crisper on the treatment of diseases (Review)

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Introduction: Background; Today, efforts to achieve technology in various fields are increasing. One of the fields that has attracted a lot of attention is genetic engineering and gene therapy. The genome is the command post of living organisms, so in order to change the structure of organisms, it is necessary to make changes in their genes. Crisper is a tool for gene modification and the purpose of this article is to review the effect of crisper on the treatment of various diseases.

Methods: Research MethodØ› Relevant information was searched from Pub med, Scopus, Google Scholer databases; And data analysis was performed qualitatively.

Results: findings; Crispers are used in many different ways today. One of the uses of Crisper is to use them in diseases including cancer. Crisper is an adaptive immune system in bacteria that enables them to detect virus DNA and then destroy it. It is part of the Crisper system called cas9, which has the ability to search, cut, and transform virus DNA in a specific way. This technology allows scientists to make changes in cell DNA. The cas9 protein is an enzyme for DNA cleavage that allows it to detect genomes in cells.

Conclusion: Conclusion; Crispers can be used in various fields such as antibiotic production and in agriculture by changing traits such as flower color. Biologists began large-scale experiments not only because of Crisper's great abilities but also because Crisper is more cost-effective than other genome editing methods.

Keywords: Keywords; DNA evolution, genome modification, Crisper, biotechnology, Cas9

The effect of NaCl and salicylic acid on total phenolic contents in suspension culture of Nitraria schoberi (Research Paper)

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Introduction: Nitraria schoberi is a medicinal plant with antioxidant, antifungal, antimicrobial, anti-inflammatory, and anti-viral properties. This plant is also tolerant to salinity and drought. Cell suspension culture is one of the most ideal methods for producing secondary metabolites, but they seldom produce sufficient amounts of the required secondary metabolites without proper elicitors. Elicitors are biotic or abiotic molecules that induce a signal across plant cells which, in turn, stimulate secondary metabolic pathways and downstream transcription factors in response to the external stimuli thus resulting in the production of secondary metabolites. The main aim of this study was to perform elicitation in cell suspension culture of N. schoberi to detect the production of total phenolic contents.

Methods: In order to achieve that goal, hypocotyls and cotyledonary leaves of N. schoberi as explants were cultured in different callus induction media. At the next step, the calli belonging to the best callus induction medium were transferred to different cell suspension cultures containing elicitors including Sodium Chloride (NaCl) and Salicylic acid (SA) alone or in combination with each other. Total phenolic contents in treatments were measured using a spectrophotometer (absorbance at 765 nm and 430 nm, respectively).

Results: Although callus induction was observed in all treatments, the maximum fresh weight (7.6 g) and dry weight (3.7 g) were obtained in MS medium supplemented with 2, 4-dichrolophenoxyacetic acid (2,4- D) and 1-naphthalene acetic acid (NAA) both at 0.5 mg/L. The highest total phenolic content (62.2 mg/g) was detected in suspension culture containing 100 mÂµ NaCl and 50 MÂµ SA.

Conclusion: . In conclusion, elicitation in suspension culture of N. schoberi can be an effective method for increasing the production of secondary metabolites (phenolic compounds).

Keywords: Elicitor, Medicinal plants, Secondary metabolites, Suspension culture

The Effect of The Antibiotic Ciprofloxacin on The Growth of Pseudomonas Aeruginosa (Research Paper)

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Introduction: The genus Pseudomonas consists of more than 120 species that are ubiquitous in moist environments such as water and soil ecosystems and pathogenic to plants, animals and humans. Within the Pseudomonas species, P. aeruginosa is most frequently associated with causing human infection; however, it naturally exists in the environment. The bacterium is regarded as an opportunistic pathogen, primarily causing nosocomial infections in immunocompromised patients. P. aeruginosa is rarely associated with causing chronic infections in previously healthy patients, although fatal cases of P. aeruginosa infections in previously healthy people have been reported. Ciprofloxacin is a broad-spectrum fluoroquinolone antibacterial agent. Since its introduction in the 1980s, most Gram-negative bacteria have remained highly susceptible to this agent in vitro; Gram-positive bacteria are generally susceptible or moderately susceptible. Ciprofloxacin attains therapeutic concentrations in most tissues and body fluids. The results of clinical trials with Ciprofloxacin have confirmed its clinical efficacy and low potential for adverse effects. This study aimed to investigate the effect of the antibiotic ciprofloxacin on the growth of Pseudomonas aeruginosa.

Methods: To investigate the effect of the antibiotic ciprofloxacin on the growth of Pseudomonas aeruginosa, Pseudomonas aeruginosa was prepared and cultured, then the bacterial suspension of Pseudomonas aeruginosa and ciprofloxacin was selected as the antibiotic used. Finally, ciprofloxacin was used to determine the MIC and MBC of Pseudomonas aeruginosa on microdilution.

Results: The results showed to evaluate the effect of the antibiotic ciprofloxacin on the growth of Pseudomonas aeruginosa, a microdilution method was used to evaluate the effect of the antibiotic ciprofloxacin on Pseudomonas aeruginosa in tubes containing Mueller Hinton Brot. And microbial suspension of ciprofloxacin antibiotic dilutions including (4000, 2000, 1000, 500, 250, 125, 62, 31, 16) ml/Âµg were prepared. The combined MICs and MBCs were then 16 ml / Âµg and 31 ml / Âµg, respectively.

Conclusion: Finally, the results of a laboratory study showed the effect of the antibiotic ciprofloxacin on the growth of Pseudomonas aeruginosa showed that the growth of Pseudomonas aeruginosa in the tube at a concentration of 16 ml / Âµg was positive in both cases, in the tube and plate. Also, the growth of

Pseudomonas aeruginosa a concentration of 31 ml / Âµg was positive in plate and, negative in the tube.

Keywords: Pseudomonas aeruginosa, ciprofloxacin, antibiotic, MIC, MBC

The effectiveness of biological and synthetic dressings from burn wounds of patients admitted to the burn ward of Ibn Sina Hospital in Shiraz (Research Paper)

zeinab sadat moosavi fard,[1,*]

1.

Introduction: Over time, many scientific and practical studies have been conducted in the field of burn wound care, including a variety of dressings. Dressing is generally done in two new and traditional ways in the care of burn wounds. Various types of new dressings such as biological and synthetic dressings are currently available. Modern dressings are thought to facilitate wound healing and do not have the limitations of traditional dressings. On the other hand, studies show that the cost of caring for burn patients is high. In this regard, cost-effectiveness analysis of care can help nurses to eliminate multiple approaches, choose measures that are appropriate for the patient and at the same time cost effective. The aim of this study was to evaluate the cost-effectiveness of biological, synthetic and traditional dressings in nursing care of burn wounds.

Methods: The present study is a clinical trial that was performed on 45 people with second degree burn wounds hospitalized in the burn ward of Ibn Sina Educational and Medical Center in Shiraz for 4 months in 2009. The study population was patients admitted to this center and among them, people who had the characteristics of the study units after informing the family about the research and obtaining written consent were selected as a sample and were randomly divided into two experimental groups and a control group. In experimental group A, 15 patients were treated with synthetic dressings, in group B, 15 patients were treated with biological dressings and in the control group, 15 patients were treated with traditional dressings. Duration of hospitalization, time of onset of healing, pain intensity, infection rate, direct and indirect costs were assessed using research tools including checklist and questionnaire. Analyzes were performed using SPSS software and descriptive and inferential tests (Chi-square-Kruskal-Wallis).

Results: The results showed that there was a significant difference between the three dressing methods in terms of length of hospital stay, time of onset of healing, pain intensity, direct and indirect costs ($P < 0.001$), meaning that in two synthetic groups compared to the other two groups, healing It happened earlier, the length of hospital stay and the severity of the pain were shorter, and less direct and indirect costs were incurred. There was no significant difference between the three dressing methods in terms of infection rate.

Conclusion: In this study, our hypothesis that there is a statistical difference between the three dressing methods in terms of cost and effectiveness was confirmed. This means that synthetic dressings were more cost effective than other dressings. This shows that not using new products and methods is not

reasonable just because of the high cost of Rials and it is necessary to pay more attention to the cost-effectiveness of new methods in this regard.

Keywords: biological dressing, synthetic dressings, burn wounds

The Emerging Role of Polymeric Microparticles as an Effective Therapeutic Strategies for Cancer (Review)

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Introduction: Microparticles (MPs) are spherical particles with dimensions in the micron range of 1 Î¼m to 1000 Î¼m that have been made of poly lactic-co-glycolic acid (PLGA), polylactic acid (PLA), polyglycolic acid (PGA), polyhydroxy alkanoates (PHA), and polyÎµ-caprolactone (PCL) by interfacial tension of immiscible liquid phases. Polymeric MPs (p-MPs) have been widely developed as drug delivery systems and also, most p-MPs are made using biocompatible and biodegradable polymers, which may decay under physiological settings and release the medication in a regulated way. Over the last several decades, encapsulating both hydrophilic and hydrophobic compounds, giving them a broad variety of therapeutic uses. The release of medicine from p-MPs shows several benefits compared with the traditional drug delivery methods, which include their ability to adjust the rate of drugs release for a long time and their capacity to reduce drug toxicity. The numerous advantages of injecting encapsulated pharmaceuticals into p-MPs serve as the foundation for a variety of future medicinal undertakings. This study shows their applications in the treatment of diseases.

Methods: The articles we reviewed used a variety of methods, the most common was the statistical analysis performed using NOVA by Graph pad prim software.

Results: The preparation of MPs was performed via solid-oil-water (s/o/w) modified double emulsification method. The release of drugs from p-MPs shows their ability to modulate the rate of drugs release for a long period. The extensive benefits of the administration of encapsulated drugs into p-MPs serve as the foundation for many future medical endeavors. Over the years, a wide range of procedures for preparing microparticles of drug delivery applications

has been developed, resulting in a wide range of morphologies, architectures, and size ranges. Emulsificationâ€“solvent evaporation is the most commonly used method for producing nano-/microparticles. Adjusting the viscosity of the organic/aqueous phases, the homogenization speed, and the emulsifier concentration allows for customizable particle size. In Oncologic disease chemotherapeutic encapsulated in polymeric microparticles provide a safe platform for achieving a prolonged release in malignant tissue, reducing the need for large medication doses and their potentially hazardous side effects. So, in the brain, it's critical to limit the number of procedures a patient undergoes, biodegradable microparticles could be an ideal therapeutic device since they not only have favorable release kinetics but also allow for the encapsulation of a large enough dosage to assure continuous therapeutic dose exposure. According to new vaccine techniques, p-MPs loaded with antigens against bacterial diseases such as Vibrio cholerae, Pseudomonas aeruginosa, and Bordetella pertussis provide a robust and long-lasting immune response.

Conclusion: The manageable of p-MPs properties (including crystallinity and degradation rates) the low toxicity, the variety of production procedures, and convenience and low cost of manufacture make them an effective strategy. Due to their superior biodegradability and biocompatibility, the use of MPs based on PLA, PLGA, and similar polymers and copolymers in the field of sustained release of medicines has recently become a major subject of research. The methods for fabricating such systems proved to be extremely adaptable. By modifying some of the experimental factors related to the preparation process, improved drug release behavior, various particle size-structure properties, and loading capacities can be accomplished in this manner. Despite substantial development in the field of microencapsulation, several problems remain. The development of less expensive biopolymers for microencapsulation technologies, as well as the development of appropriate evaluation procedures, should be prioritized, especially for bio adhesive microsystems. As a result, in the future, in-depth investigations of both the technological and biological characteristics of these systems will be required to build safe and efficient systems.

Keywords: Polymeric Microparticles (p-MPs), Therapeutic, Carcinoma, Oncologic disease, Microparticles

The evaluation of FKBP5 regulation through Pancreatic Cancer by informatics study (Research Paper)

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Introduction: Introduction. Pancreatic cancer (PAC) is the twelfth most commonly diagnosed cancer and the third leading cancer in the world. PAC, although relatively rare, is very deadly and is usually diagnosed in advanced stages. Prevention and early diagnosis are important factors in patientsâ€™ survival.

Methods: Methods. The GSE16515 was selected from Gene Expression Omnibus (GEO) dataset in order to detect differences in gene expression in which the experiment was performed between the two groups of tumor and normal samples. Using GeneMANIA, we obtained the highest genetic association among FKBP5, HSP90AA1 and HSP90AB1 genes.

Results: Results. The impaired expression of the FKBP5 gene causes glucose resistance to the insulin hormone, and this resistance eventually leads to an increase in blood sugar levels and a decrease in glycogen, the stored form of glucose. The data showed that decreased expression of FKBP5 in human adipose tissue has a potential role in glucose and lipid metabolism, adipogenesis, and type 2 diabetes (T2D). The expression level of FKBP5 gene in people with pancreatic cancer is lower than normal people and the expression of this gene in these people is 35.69 TPM while in normal people the expression of gene is 39.05 TPM. Diabetes eventually leads to unlimited growth of pancreatic cells due to dysfunctional insulin combined with glucose biosynthesis (glycogen depletion) and pancreatic cancer will accrue. This gene has a significant effect on other common cancers while upregulation such as acute myeloid leukemia and prostate adenocarcinoma. The two genes HSP90AA1 and HSP9OAB1 had the highest genetic association with FKBP5, and increased expression in these two genes causes unlimited growth of the pancreatic cells. HSP90AA1 and HSP90AB1 genes were expressed in tumor samples with 333.81 TPM and 482.37 TPM, respectively; while 93.45 TPM and 261.4 TPM were reported in normal samples.

Conclusion: Conclusion. It is concluded that type 2 diabetes is both a consequence and a cause of pancreatic cancer. It could be said that if a triangle is considered, the three corners of this triangle are PAC, T2D, FKBP5.

Keywords: Keywords: FKBP5, PAC, T2D, HSP90AA1, HSP90AB1

The impact of rs9341070 and miR-122 interaction on ESR1 gene through Breast cancer (Review)

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Introduction: Breast cancer is the most common malignancy among women worldwide. Genetic alterations, including Single Nucleotide Polymorphisms (SNPs) have been identified as important factors in understanding carcinogenesis. Numerous studies have shown their association with microRNA binding. MicroRNAs bind to 3'UTR of target mRNAs, blocking translation or, in rare cases, destroying target mRNAs and regulate various biological processes such as cell differentiation, cellular metabolism, immune response, and apoptosis. Since the expression level of miRNAs varies between normal and cancer cells, they are proposed as clinical biomarkers and even therapeutic targets in cancers. The aim of this study was to investigate the effect of SNP:rs9341070 on has-miR-122-5p binding to Estrogen Receptor Alpha (ESR1) gene and its suppressive function.

Methods: To perform this study, the desired gene was selected through literature mining of previous studies. The NCBI database was used to obtain more information about SNP: rs9341070. The miRdSNP database was also used to investigate the association between rs9341070, ESR1 gene and has-miR-122-5p in breast cancer. In the following, the miRNASNP-v3 database was applied to study the presence of rs9341070 in 3Â´-UTR region of ESR1 gene and its interaction with the has-miR-122-5p. Through the studies, the gene, SNP and microRNA, were selected as ESR1, rs9341070, and has-miR-122-5p respectively.

Results: The results from research in databases showed that the occurrence of rs9341070 in ESR1 3Â´-UTR region is a risk factor in breast cancer. The hsa-miR-122-5p is a tumor suppressor and inhibits cancer cell proliferation and tumorigenesis in breast tissue. The has-miR-122-5p binds to mRNA and prevents the expression of ESR1 gene. Occurrence of rs9341070 at the seed match of miR to ESR1 gene by converting the C to T makes the miRNA to lose the mRNA. It makes an increase in ESR1 gene expression and tumorigenesis in this tissue. The rs9341070 prevents the binding of miR-122 to ESR1 gene in breast tissue. As a result, the function of tumor suppression and inhibition of cancer cell growth is impaired. It results in upregulation in ESR1 and progression of breast cancer.

Conclusion: According to the findings, the occurrence of SNPs in 3'-UTR disrupts the regulatory action of microRNAs on target mRNAs and potentially contribute to cancer and other chronic diseases. The rs9341070 is associated with various aspects of breast cancer and plays an important role in preoperative assessments as a marker in predicting the progression of breast cancer metastasis. The microRNAs can also potentially be predictive as therapeutic biomarkers that allow patients to benefit from personalized medicine. Our study showed that miR-122 expression level and its interaction with ESR1 gene play important roles in inhibiting tumorigenesis, development and progression of breast cancer and may be used as a biomarker for diagnosis and prognosis and even a target for breast cancer treatment. However, experimentally researches are needed to confirm these results in patients with breast cancer.

Keywords: Cancer, 3â€™UTR, MicroRNA, SNP

The in silico analysis of phytochemicals for determining anti-cancer compunds that target CYP1B1 and CASP3 (Research Paper)

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Introduction: The caspase family of proteases plays a critical role in apoptosis. In human cancer patients, higher levels of activated caspase 3 in tumor tissues are associated with an increased rate of deaths.It has been indicated that inhibition of caspase-3 affects lung cancer sensitivity to radiation. CYP1B1 contributes to the metabolic activation of some environmental procarcinogens. It plays role in the metabolism of 17Î²-estradiol. The overexpression of CASP3 and CYP1B1 is also observed in Cervical and Renal cancer, respectively. As a result, they can be suitable targets for cancer treatment.Therefore, in this study, molecular docking was used to investigate the binding energy of herbal compounds in some Bangladeshn native plants to see whether they are appropriate inhibitors for CASP3 and CYP1B1.

Methods: To acquire the information regarding medicinal plants and their active compounds, a research was conducted using (www.medicinalplantbd.com) database. We investigated the interaction between plant-based compounds and human proteins using STITCH 4.0 (http://stitch.embl.de/). The X-ray 3D structure of CASP3 and CYP1B1 was obtained from the Protein Data Bank (PDB). Moreover, the chemical structures of these small molecules were obtained from the Human Metabolome Database(https://hmdb.ca/). Molecular docking was executed using Autodock vina 1.1.2 software to find out the affinity between molecules and evaluate binding energies in the complex.

Results: Among Chrysoeriol, Myricetin, Isorhamnetin, Quercetin and Kaempferol, Chrysoeriol gains the most affinity score with -8.8 (kcal/mol) in interaction with CYP1B1. As far as CASP3 is concerned, the best affinity was related to Î²-sitosterol with the affinity of 9.74 kcal/mol, followed by Oleanolic acid, and Betulinic acid with the affinity of -9.35 kcal/mol, -8.94 kcal/mol, respectively.

Conclusion: To conclude, Ficus racemosa L. containng Î²-sitosterol has theraputic usage to target CASP3, and Nymphaea nouchali Burm.f. var. mutandaensis can be the most effective plant that targets CYP1B1, as it includes Chrysoeriol, Isorhamnetin, and Kaempferol.

Keywords: CYP1B1, caspase 3, medical plants, Chrysoeriol , Î²-sitosterol

The relationship between Toxocara species seropositivity and allergic skin disorders: a systematic review and meta-analysis (Review)

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Introduction: Allergic skin diseases (ASDs) are a group of itchy, inflammatory skin conditions with substantial morbidity worldwide and negative impact on the quality of life of patients and their families. Atopic dermatitis, prurigo, pruritus, eczema and urticaria are among the most common ASDs. These disorders affect up to 20% of children and up to 5% of adults globally, and their prevalence is increasing worldwide, especially in low-income countries. In routine clinical practice, in the majority of cases the causes of these disorders are not easily identifiable. It has been demonstrated that both genetic and environmental factors play important roles in the development of ASDs. Moreover, it is assumed that infections, including internal parasitic infections, could be an underlying cause of some ASDs . Toxocara infection is a globally distributed zoonotic disease with an estimated of 2 billion at-risk people worldwide. Human toxocariasis is caused by the larval stage of Toxocara canis and Toxocara cati and rarely by other Toxocara species, which are intestinal nematodes founded in canids and felids as definitive hosts. Human infection occurs by the ingestion of infective eggs of Toxocara through contaminated vegetables, water, soil and hands or by direct contact with puppies and kittens, and children are more at risk for infection. Humans are accidental hosts for Toxocara, and after hatching in the intestine, larvae migrate to other organs or tissues, including the lungs, liver, muscles and central nervous system, without developing into the adult form. Migrating larvae are associated with peripheral blood hypereosinophilia and several clinical manifestations, mostly categorized as ocular larva migrans (OLM), visceral larva migrans (VLM) and neurologic or covert toxocariasis. Epidemiological evidence suggests that helminth parasites, especially those known as nematodes, have protective effects against atopy and allergic diseases, as allergic diseases are rare in regions with high helminth parasite exposure and common in areas with low or reduced helminth exposure. In contrast to other helminthic infections, it is assumed that Toxocara infection (which has an incomplete life cycle in humans) could trigger the inception of allergic diseases, including asthma, wheezing and atopy. In past years a growing number of studies investigated the possible association between Toxocara infection and the risk of ASDs, however, the results are conflicting. Here, for the first time, we performed a systematic review and metaanalysis on all studies published to date to gain a better understanding regarding the association between Toxocara infection and the development of ASDs. The results of this study may be helpful for clinicians, who should consider toxocariasis as a potential cause of ASDs, allowing for early diagnosis and treatment of ASDs.

Methods: We searched the MEDLINE, ScienceDirect, Scopus, Web of Science and Google Scholar databases to 15 May 2021 to identify the relevant studies. We used a random effects meta-analysis model to generate the pooled odds ratio (OR) and 95% confidence intervals (CIs).

Results: Fifteen studies, including eight studies with a caseâ€“control design (735 patients and 1342 controls) and seven studies with a cross-sectional design (a total of 4804 participants, 1302 individuals with ASDs and 3502 without ASDs), were included in the meta-analysis. We found an increased risk for ASDs in individuals with Toxocara seropositivity (OR 1.75 [95% CI 1.16 to 2.64]). Subanalysis showed that Toxocara seropositivity was significantly associated with urticaria (OR 2.97 [95% CI 1.53 to 5.76]), however, it was not significantly associated with atopy (OR 1.08 [95% CI 0.55 to 2.15]) and eczema (OR 1.62 [95% CI 0.95 to 2.78]). Moreover, the pooled ORs were 2.34 (95% CI 1.32 to 4.15) and 1.27 (95% CI 0.69 to 2.35) for case-control and cross-sectional studies, respectively.

Conclusion: The results of our study support hypotheses regarding the existence of a positive relationship between Toxocara infection and allergic disorders, although this association should be further investigated by longitudinal and mechanism studies.

Keywords: allergy, meta-analysis, skin disorders, Toxocara infection, urticaria

The Role of Cancers on the COVID-19 Incidence and Outcomes: A comprehensive review study of the current knowledge (Review)

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Introduction: Today the novel coronavirus disease (COVID-19) had become a great worldwide disaster. During the pandemic, cancer patients are a high-risk group in getting the infection and have severe outcomes. In the current study, we performed a systematic review to determine the COVID-19â€™s outcomes severity in cancer patients.

Methods: A comprehensive systematic search was conducted in electronic databases including Embase, Pubmed, Scopus, and Web of science with the keywords â€œCancerâ€□, â€œCOVID-19â€• and all other related MeSH terms up to December 2021. Cohort studies that investigated the cancer patients in comparison with non-cancer patients were included in this review, the studies that did not mention cancer patients' outcomes of COVID-19â€™s infection were excluded.

Results: According to the included studies (n=11), the analysis of 5,619 patients (2,032 with active cancer) determined that cancer patients are significantly more likely to admit to the ICU and the mortality rate is higher in them. Being male and receiving received any cancer therapy within 4 weeks before the onset of the COVID-19 symptoms blurts severer outcomes of the disease in comparison with the patients who did not do any cancer therapy. Chemotherapy was the most common therapeutic method was done for cancer patients and an obvious relationship was observed between the chemotherapy and the COVID-19â€™s outcomes severity; In the other words, chemotherapy could be a risk factor for the outcomes severity and deaths due to COVID-19. Interestingly, the studies expressed that immunosuppressive therapies may not worsen the outcomes of COVID-19, however, this could be due to treatment side effects. Moreover, patients with breast cancer were the most probable group of cancer patients in getting COVID-19 infection.

Conclusion: Due to our systematic study, there are more severe outcomes of COVID-19 in cancer patients, in comparison with non-cancer patients, and more attention is needed.

Keywords: COVID-19, Cancer, Cancer Therapy

The role of ISH technique in the field of molecular biotechnology (Review)

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Introduction: Changes in the genome and proteome of cells disrupt normal cellular control mechanisms. Using biotechnology methods, these molecular errors can be identified and appropriate therapies selected. In situ hybridization (ISH) is one of these techniques. In situ hybridization (ISH) is a type of hybridization that uses a complementary DNA marker, RNA, or modified nucleic acid strand (probe) to concentrate a specific DNA or RNA sequence in a portion or part of tissue (in situ). DNA ISH can be used in medical diagnosis to assess chromosomal integrity. ISH RNA is used to measure and localize RNAs (mRNAs, lncRNAs, and miRNAs) in tissue sections, cells, and circulating tumor cells (CTCs).

Methods: In this review study, searches were performed on PubMed, Medline, Google Scholar, Scopus and ISI electronic and scientific databases and valid related articles were searched using the keywords In situ hybridization (ISH) and molecular biotechnology.

Results: Certainly, using ISH technique, important steps can be taken in the field of medical science and biotechnology of cancer.

Conclusion: ISH technique has increased the knowledge of researchers about molecular events, so according to the performance of ISH technique can be used in research, diagnosis and early treatment of cancer and other emerging infectious diseases.

Keywords: In situ hybridization (ISH), molecular biotechnology, diagnosis

The role of leukemia inhibitory factor in cardiovascular diseases in leukemia patients: diagnostic and prognostic approach (Review)

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Introduction: Leukemia is a group of malignancies, that usually begins in the bone marrow and results in high numbers of abnormal blood cells; it is one of the leading causes of death. Chemotherapy drugs are used to treat leukemia by blocking and activating a series of pathways. Some of these drugs cause side effects, such as cardiovascular disease (CVD) by disrupting the endothelial cells. Leukemia inhibitory factor (LIF) is a secretory glycoprotein, that belongs to the IL-6 family. IL-6 has been shown to be involved in heart protection, creating blood vessels and cell-to-cell attachment in the heart, and promoting the proliferation of cardio myocytes. Evidence also shows, that LIF affects the heart muscle and protects the heart muscle against Reactive oxygen species (ROS) damage. By binding to its specific receptor, LIF targets the damaged myocardium through some signaling pathways, preserving EC structure and angiogenesis; it may be a good option for the CVD treatment. Therefore, in this study we investigated the LIF role in the pathogenesis of CVD caused by treatment in the leukemia patients.

Methods: This article is a review of researches done during 1995-2021 in the PubMed, EMBASE and Scopus database. The following keywords were used for this article: "Leukemia", "Leukemia inhibitory factor", "Cardiovascular disease", "Angiogenesis", "Endothelial Dysfunction".

Results: LIF that improves CVD by activating the JAK / STAT, PI3K / AKT, and MEK / ERK signaling pathways. The activating factors of angiogenesis pathway such as VEGF and VE-Cadherin are expressed through the LIF activation pathway. Activation of angiogenesis due to LIF may lead to malignant leukemia.

Conclusion: LIF has a dual role; it can be considered for activating the signaling pathways and improves the heart function. LIF-induced angiogenesis may lead to the development of leukemia. The relationship between the treatment strategies and LIF signaling pathways in different tissues, needs to be studied more extensively.

Keywords: Leukemia inhibitory factor, Leukemia, Endothelial cell, Diagnosis

The role of luteinizing hormone and its associated genes in progression of breast cancer: a bioinformatics approach (Research Paper)

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Introduction: Breast cancer is a major public health problem for women, and in many cases distant metastases and recurrence are the leading cause of death among patients. About 80% of diagnosed breast cancers are hormone-dependent, commonly hormones secreted by the hypothalamic-pituitary-gonadal (HPG) axis. These hormones, as well as regulating the reproductive system functions, can stimulate tumor development and progression in the tissues that have receptors for these hormones. The direct correlation of circulating levels of gonadotrophins (LH, FSH, and HCG) with tumor progression in an invivo model of breast cancer has been reported. In addition other investigations have shown that luteinizing hormone (LH) modulates the expression of a set of genes associated with tumorigenesis in breast cancer cell lines. The aim of the present study was elucidate the role of the LH associated genes on breast cancer metastasis using bioinformatics approach.

Methods: STITCH database was utilized to find direct protein targets (DPT) of LH receptor and CTD database was used to identify DPT-associated genes. Then STRING database was employed to construct an interaction network of DPTs and DPT-associated genes. Resulted network was analyzed Using Cytoscape v3.7.0. to identify the most potentially effective genes (hubs and bottlenecks). Also, MCODE algorithm was used to screen the modules and sub-networks. Finally, the expression levels of identified genes were subsequently investigated from early stage to metastasis (stage: I â€“ IV) in breast tumor tissues based on TCGA data reported in UALCAN.

Results: Nine DPT and 1456 DPT-associated genes were identified for LH receptor. Their network analysis based on degree and betweenness parameters identified overall 22 hubs and bottlenecks as the most potentially effective genes. MCODE analysis identified 30 clusters from the network that among them cluster 1 with the highest score was containing 49 nodes and 1111 edges in which UBB, UBC, UBA52, EEF2, EEF1A1, and RPS27A were identified as common genes between nodes of cluster 1 and hub and bottleneck genes. TCGA data showed significant decreasing trend in expression levels of EEF2, EEF1A1, and RPS27A genes from stage I to IV in breast tumor tissue. While, increment of UBB expression level and not significant changes for UBC and UBA52 expression levels were observed during breast tumor progression from stage I to IV.

Conclusion: We identified a four-gene set (UBB, EEF2, EEF1A1, and RPS27A) associated with LH receptor that expressed in breast tumor. Down-

regulation of EEF2, EEF1A1, and RPS27A from stage I to IV can suggest their tumor inhibitor role in breast tissue whereas up-regulation of UBB may offer its role as a tumor activator during breast tumor progression from early stage to metastasis. But, for verification of these bioinformatics results experimental study is needed.

Keywords: breast cancer, luteinizing hormone, tumor progression, bioinformatics

The role of oncolytic viruses in cancer therapy (Review)

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Introduction: Oncolytic viruses (OVs) are described as genetically engineered or natural viruses that are used to treat a variety of cancers, especially in advanced stages. OVs selectively proliferate in cancer cells without damaging normal tissues and lead to tumor regression by inducing a host anti-tumor immune response. In general, viruses provide a unique host for cancer treatment by facilitating genomic manipulation to increase viral tropism in neoplastic cells, increase selective proliferation, modify viral pathogenesis, and induce antitumor immunity. In addition, genetic engineering of additional genes to enhance anti-tumor immunity, increase the sensitivity of tumor cells to ionizing radiation and ultimately increase patient immunity can be considered as the main and important characteristics of oncolytic viruses. Among the various viruses, including adenovirus, herpesvirus, poxviruses, coxsackie A virus, Newcastle disease virus, reovirus, picornavirus, and vaccinia virus, that have been developed for the treatment of oncolytic diseases, the most common OVs used in clinical trials are adenovirus, HSV-1, reovirus, picornavirus, and poxviruses.

Methods: An overview of the organized literature was conducted in the PubMed database. Out of 4120 articles from 2000 to 2022, articles related to the role of Oncolytic viruses in cancer treatment were screened and studied.

Results: Worldwide, three OVs have been approved for the treatment of advanced cancers. The first is Rigvir, an RNA virus derived from the ECHO-7 picornavirus strain. Then, a genetically modified adenovirus called H101 was approved for the treatment of nasopharyngeal carcinoma in combination with cytotoxic chemotherapy. Finally, Talimogene laherparepvec (T-VEC), an attenuated herpes simplex virus type 1 (HSV-1), was approved in 2015 by the US Food and Drug Administration for the treatment of melanoma patients. Currently, T- VEC is used in many clinical trials. Genetic manipulation has occurred in the HSV-1 genome in order to selectively replicate the virus in cancer cells, attenuate pathogenesis, and enhance the host antitumor immune response. For this purpose, deletion of É£34.5 and á¼€47 genes can be mentioned, which the É£34.5 gene prevents from stopping the protein synthesis of host cells during viral infection. Therefore, by deleting this gene, the virus cannot replicate in normal cells, and on the other hand, by inhibiting the reduction of MHC class I expression, the immune response against cancer cells is increased. Deletion of the á¼€47 gene also leads to early expression of the US11 gene and increase in viral replication in cancer cells. Another important

change in HSV-1 is the placement of a transgene called GM-CSF at the É£34.5 deletion site. GM-CSF is a human macrophage granulocyte colony stimulating factor that is thought to aid in the uptake and maturation of dendritic cells and ultimately lead to the production of immune stimuli. One of the important issues in the clinical development of OVs is choosing how to present the virus to the cancer patient. In early studies, the direct intratumoral (IT) injection was used, which may be challenging for visceral and central nervous system (CNS) tumors. Another strategy is intravenous injection, which seems simple and can target multiple metastatic areas, but may be complicated by rapid dilution in the circulation, neutralization by antiviral antibodies and other serum proteins. It should be noted that the most common side effects of OVs are fever, fatigue, chills, nausea / vomiting, flu symptoms, low pain at the injection site, and other common side effects, all of which have low-grade symptoms. Most studies of cancer treatment with OVs are monotherapy, but there are studies based on combination therapy. Contrary to expectations, most combined studies were in the form of OV evaluation and cytotoxic chemotherapy, while treatment of OVs and immunotherapy has received less research.

Conclusion: Although significant progress has been made to date in the development of oncolytic viruses as a treatment for cancer, but further research is needed to optimally select viruses, describe the clinical effects of OVs, how the virus is delivered to the tumor site, and immunogenicity. However, there is growing evidence that this approach is potentially promising for the treatment of human cancers

Keywords: Oncolytic virus, Tumors, cancer therapy, Herpes simplex virus type 1, Adenovirus

The role of PIK3CA gene mutations in breast cancer (Research Paper)

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Introduction: Today, breast cancer is one of the most common cancers among women and at the same time one of the most important diseases in the world. Epidermal growth factor 2 (HER2) receptor, a member of the epidermal growth factor (EGF) family , which is highly expressed in a large proportion of breast cancers. Trastuzumab or Herceptin is a monoclonal antibody that acts as an anti-HER2 agent for targeted therapies , Patients treated with HER-2 overexpression are treated, Therefore, for some HER2 + breast cancer patients, trastuzumab is not beneficial and breast cancer in these patients spreads or spreads over time. . The PI3K pathway is a family of lipid kinases that phosphorylates the 3OH group of phosphatidylinositol, PI3K has alpha (Î±), beta (Î²) and gamma (Î³) subunits. The alpha subunit (PI3KCA) plays a much more important role in the transmission of cancer messages, and various studies have been performed on it. Activation of PI3K activates a message cascade that promotes the growth, survival, and metabolism of cancer cells. The PIK3CA gene encodes the alpha catalytic subunit of the PI3K enzyme. PIK3CA mutations indicate resistance to trastuzumab therapy by activation of the PI3K / AKT pathway. The aim of this study was to evaluate the frequency of mutations in common points of PIK3CA gene, including exons 9 and 20, in HER2 + breast cancer patients resistant to trastuzumab , compared with patients who responded to treatment.

Methods: In this case-control study, a number of control and paraffin-embedded breast tissue samples from HER2 + ductal carcinoma patients who were treated with Transtuzumab for one year. After examining the variables to be studied by the oncologist, samples were collected from the Breast Cancer Research Institute and the tumor bank of Imam Khomeini Hospital in Tehran and examined. The age range of patients was between 27 and 67 years and their mean age was 47 years . These patients were evaluated for age and type, size, grade and stage of the tumor and the number of lymph nodes involved, and Stage 4 patients were not included in the study. Also information about the presence of tumor markers such as HER2, ER, PR . Patients' medication regimens were also evaluated. DNA extraction was performed from the samples and PCR test was optimized using breast cancer tissue samples expressed in exon 9 and exon 20 of PI3KCA gene and positive and negative control along with the size of the marker. Primers were optimized and used. Finally, Sanger method was used to sequence exons 9 and 20 of PIK3CA gene in this study, which was performed by Macrogen Company of South Korea.

Results: Out of 52 patients included in the plan, 23 (44%) were identified as herceptin resistant and 29 (55%) as sensitive to herceptin.The age range of patients was between 27 and 67 years and their mean age was 47 years. All patients were HER2 (+3) and had received herceptin.30 patients (57%) had ER + tumor marker and 24 patients (46%) had PR + tumor marker.In this study,

nucleotide changes including 67039GËƒT on exon 9 and 86860CËƒG on exon 20 were observed. The frequency of G70T 67039 in the group of susceptible patients was 7.7% but this mutation was not observed in the group of resistant patients.Odds ratio for this jump was 0.12 (95% CI: 0.1983 to 3.2842) and P = 0.1.. The frequency of 86860CGG on exon 20 was 17.4% in the group of resistant patients and 20.7% in the group of susceptible patients.The Oddsratio ratio for this mutation was 0.8 (95% CI: 0.0062 to 2.3620) and P = 0.7.

Conclusion: Trastuzumab is in fact an effective and essential anti-cancer drug in the treatment of people with breast cancer. A significant number of patients after initial treatment with a diet containing trastuzumab, their disease progresses progressively and requires the addition (continuation) of the treatment process. The results of this study showed a mutation in PIK3CA gene in HER2-positive breast cancer patients treated with trastuzumab, but the study of the presence of these mutations in two groups resistant and sensitive to trastuzumab and calculating the amount of these mutations in both groups, a significant relationship between this Mutations with resistance to trastuzumab treatment were not observed. The mutations found in this study included 67039GËƒT on exon 9 and 86860CG on exon 20, of which 67039GËƒT was not observed in the group of sensitive patients with a frequency of 7.7% and in the group of resistant patients.

Keywords: Transtomazob , HER2, PI3K, Breast cancer, , Mutations

The role of transgenic plants in coping with acute respiratory syndrome SARS-Cov2 (Review)

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Introduction: Currently, more than 45% of deaths in developing countries are due to infectious diseases. The most important way to prevent these diseases is to vaccinate people. But more than 30 million children worldwide have not yet been immunized against these preventable and treatable diseases. Because current methods of vaccine production are technologically complex and therefore expensive. In particular, the conditions and facilities of packing, storage in the cold and their transportation lead to an increase in prices. Therefore, the existence of these conditions causes a large part of the population of developing and poor countries to not have access to the vaccination process [1]. On the other hand, various antibiotics are used to treat diseases caused by viral and bacterial infections; Increasingly inappropriate use of antibiotics is increasing the resistance of bacteria to them, and this has been a concern for researchers for the past decade. For this reason, achieving new strategies to immunize the human body is based on methods of preventing infectious diseases [2]. In December 2019, a new strain of the coronavirus (SARS-CoV-2) appeared in Wuhan, leading to the development of an epidemic of acute respiratory syndrome (COV). Over a period of three months, the virus spread to more than 118,000 people in 114 countries and killed more than 4,000 people [4] [3]. With the involvement of 114 countries, the World Health Organization on March 11, 2020 declared this disease as a global epidemic [5]. Governments took control measures, aimed at delaying the spread of infection and thus reducing the strain on hospital beds, the front lines of treatment, staff, and medical resources. Reducing the rate of infection and thus reducing the total number of acute cases at any time can help prevent the collapse of national health systems. These techniques also give researchers more time to develop effective experimental methods to identify carriers of the disease, as well as find treatments to reduce the severity of symptoms and eliminate the infection more quickly. This time also allows researchers to introduce candidate vaccines to protect sections of the population that have not been exposed to the disease. Therefore, researchers working on plant applications can play an important role at this time. Existing knowledge and scientific infrastructure can be used as a tool to develop new diagnostic and therapeutic methods; Therefore, plants can be used as hosts to make such referrals over a period of several weeks, and this time seems to be economical and wise compared to the time required for cell-based systems, which may take several months to several years arrives.

Methods: 1- Resistance to coat protein (CP): This phenomenon was first reported by Sherwood and Fulto in 1982 and by Bawan et al In 1985. The concept of pathogen resistance was first reported by Sanford and Johnson in 1985, and was demonstrated in transgenic tobacco plants by Paul-Abel et al In

1986. In this study, the expression of tobacco mosaic virus (TMV) envelope protein was delayed until the onset of symptoms due to tobacco disease. Similar experiments were performed rapidly and the occurrence of this phenomenon in various viruses such as alfalfa mosaic virus (AMV), PVX and cabbage mosaic virus (CMV) was confirmed. Coating protein (CP) resistance can be widespread or limited to the RNA of viruses [16] [17]. 2- Resistance by virus replication sequence: Genes encoding protein replicase viruses can cause immunity to the disease. All plant viruses have replicase genes. Plant translocation with this method creates a high resistance that is only created against the target virus or very close strains. The mechanisms involved in resistance to replication sequences are not well understood, as they are likely to interfere with virus replication and gene expression [18]. 3- 3- Resistance due to viral motor protein: Motor protein resistance is created by competing between the motor protein produced from the transgenic plant and the virus attack to find binding sites on the host plant plasmodsmata. Thus, resistance to virus motility protein overshadows a wider range of viruses than replicase resistance [19]. 4- RNA-mediated resistance: Some methods of resistance to pathogens are genes that do not encode proteins. One of these methods is the expression of RNA heterogeneous sequences to prevent virus replication through RNA suppression [20]. RNA resistance in transgenic plants acts as a trap to prevent the production of proteins that multiply and move the virus through competition of the virus with the transgenic plant or its RNA version. This process works in different ways. In some studies, it has been reported that a transgene with inadequate DI inhibition in virus RNA reduced virus replication [21].

Results: Compared to traditional methods of vaccine production, oral herbal vaccines have low production costs, easy storage conditions, cost-effective transportation, and also provide oral immunity and are easy to use. Therefore, the medical community has a strong tendency to produce recombinant human proteins in transgenic plants. The prevailing view is that transgenic plants can produce significant amounts of low-cost antigen. The use of oral vaccines, especially when used as part of a diet, eliminates the need to train staff to administer the vaccine, but before this new method can be further developed, More research should be done on different types of antigens. The basic idea of oral plant vaccines is that humans can consume transgenic fruits or vegetables that express the antigen of a virus or bacterium in their raw form. Therefore, the eaten plant acts as an active vaccine and provides an adequate immune response against certain diseases. Many scientists call this theory simple because the different fruits of a plant express different amounts of an antigen. Therefore, in order to achieve the appropriate concentration of the desired antigen, a minimum amount of production should be considered, including storage of fruits of different plants, homogenization and dry freezing before packaging. The use of oral antigens in transgenic plants also causes unusual sensitivities in laboratory animals, which is called oral resistance. Therefore, it is necessary to determine the amount of antigen that reaches the body through the consumption of plant material is less than the amount that induces oral resistance. Oral resistance depends on the concentration and type of antigen, so when producing a protein in a transgenic plant, the issue of oral resistance

should also be considered. Also, the use of transgenic plants as bioreactors producing recombinant proteins has caused a great deal of consideration; Therefore, before transgenic organisms are released into the environment, environmental safety must be taken into account in order to separate medicinal fruits and vegetables from ordinary edible fruits and vegetables. On the other hand, the molecular farming community is very active in creating plant-based processes to produce diagnostic and therapeutic proteins to combat Covid-19 disease. The two currents of the EU Consortium on Molecular Agriculture state that their efforts will lead to the production of such targeted proteins. So we can help curb the current Covid-19 epidemic by providing accurate modeling for a quick and targeted response.

Conclusion: VLPs (Virus-like particles) vaccines with SARS-CoV-2 antigens have several advantages; Because of their size, these particles are more effectively absorbed by antigen-containing cells and stimulate the adaptive immune system, and regular protein structures can stimulate strong cellular and humoral responses to detect danger signals [28]. Therefore, VLPs based on plant viruses provide an additional layer of immunity because even protein particles cannot reproduce in humans; Therefore, large quantities of them can be produced through molecular agriculture in plants [29]. Medicago recently announced that it intends to use its platforms to rapidly produce VLP-based vaccines against SARS-CoV-2, while the exact nature of VLPs remains a mystery [30]. Virus antigens and VLPs elicit an immune response to the pathogen when exposed to the cell, while injecting recombinant antibodies to SARS-CoV-2 slows the rate of infection and allows the body to secrete its own antibodies before it can succumb to the disease [31]. Therefore, plants can be used to produce antibodies, not only as diagnostic reagents for the virus, but also as a form of inactivated immunotherapy. In addition to producing antibodies that directly kill the virus, plants can be used to produce large amounts of therapeutic antibodies. Because cytokine storms inhibit SARS-CoV-2 infection in many fatalities. The two antibodies that can be used for this purpose to treat Covid-19 are Kevzara / Sarilumab and tocilizumab / Actemra, both of which bind to the interleukin-6 (IL-6) receptor and are used to treat rheumatoid arthritis, that both of them are in the clinical trial phase of Covid -19 [33] [32].

Keywords: Transgenic plants, SARS- Cov-2, Herbal vaccines

The Use of Nanomedicine Against Hepatocellular Carcinoma (Review)

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Introduction: The most frequent type of primary liver cancer is hepatocellular carcinoma (HCC), which is also the fifth most common cancer worldwide. It has a high mortality rate, with over 600,000 people dying each year around the world. The majority of patients are diagnosed at advanced stages of the disease, when existing therapy choices are restricted and ineffective, due to the sneaky nature of HCC's progression. Treatment for HCC is based on some criteria, including the tumor stage, the patient's performance status, and the liver's functional reserve, necessitating a multidisciplinary approach. Local ablative treatments, resection, and liver transplantation are currently available treatment options for early-stage HCC. Given the high mortality rates associated with this malignancy, it is a prominent study issue to focus on to improve treatment methods. Nanoparticles (NPs) are a diverse class of materials that have been employed to battle liver cancer in a variety of ways. Inorganic NPs such as gold, silver, platinum, metal oxide, calcium, and selenium, as well as less common compounds, have all been used in drug delivery systems as a therapeutic, carrier, or imaging agent (DDS). The purpose of this study was to investigate The Use of nanomedicine against hepatocellular carcinoma.

Methods: The present study is titled The Use of Nanomedicine Against Hepatocellular Carcinoma which was done by searching scientific databases such as Science Direct, Springer, Google Scholar, PubMed.

Results: Nanoparticles are beneficial in cancer therapy, according to the findings. The use of nanotechnology in cancer detection, therapy, and management has ushered in a new era. NPs increases the intracellular concentration of medications while avoiding toxicity in healthy tissue, either through active or passive targeting. To establish and regulate drug release, the targeted NPs can be created and changed to be pH-sensitive or temperature-sensitive. NPs physicochemical properties," such as shape, size, molecular mass, and surface chemistry, also play an important role in the targeted drug delivery system. Furthermore, NPs can be tailored to the target and used to target a specific moiety. Because of unequal distribution and cytotoxicity, traditional chemotherapy and radiation therapy have significant drawbacks in terms of efficacy and adverse effects. As a result, careful dosing is essential to successfully eliminate cancer cells while minimizing damage. The medicine must cross multiple fortifications before it can reach the target spot. The metabolism of drugs is a complicated process.

Conclusion: Therefore, cutting-edge research and development in HCC nanomedicine have created a potent tool for tumor targeting that is superior to older methods. Although designing a nano-drug delivery system is a complex

process that necessitates optimizing its physicochemical properties, targeting HCC cells necessitates a thorough understanding of the challenges, such as a cirrhotic liver setting and the interaction between nanoparticles and the HCC tumor environment, that are preventing its translation into clinical practice. Nanotechnology has a number of major advantages, ranging from effective targeting to reduced systemic toxicity. Surprisingly, the most important aspect of developing HCC nanomedicine is creating nanosystems with receptor-specific ligands, such as ASGPR, GPC3, TfR, FR, and SR-B1. Several in vitro and in vivo investigations have demonstrated the efficacy of nanosystems with such targeted ligands for anti-cancer treatment. As a result, progress has been made in developing particularly targeted nano delivery systems for HCC, and this method has a lot of potential for clinical application.

Keywords: Nanomedicine, Hepatocellular Carcinoma, cancer

Transfersome nanocarriers containing antibacterial drugs as a therapeutic potential for skin infectious diseases (Research Paper)

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Introduction: Drug delivery to skin using topical ointments as a non-invasive treatment has several advantages, including effective and continuous local release as well as being easy applicable and cost-beneficial for patient. Despite of these advantages, the stratum corneum, which acts as a defense layer, prevents the penetration of small molecules smaller than 500 daltons. For larger molecules, such as organic chemicals, nanocarrier-based drug delivery systems are more suitable. Bacterial infections caused by impaired immune systems are one of the most prevalent causes of chronic skin infections, resulting in prolonged inflammation, immunological responses of host cells, infectious extension, and cytokine release at the site of the damage. Ferulic acid (FA), a chemical with a wide range of physiological effects (anti-inflammatory, antioxidant, antibacterial, anti-cancer, and anti-diabetic), protects the skin's basal structures, increases angiogenesis, and supports wound healing. For this reason, it is widely used in skin care formulations as a light protective agent, delaying the aging process of the skin and as a skin-lightening component. Here, the synthesis of a FA-transferosome is developed for proper skin delivery of FA.

Methods: FA-Transfersomes was prepared by a conventional rotary evaporation method, the appropriate weight of lipid, surfactant, and ferulic acid were dissolved in a methanol/chloroform solution (1:2, v/v) in a round-bottom flask. Thin lipid films were obtained by removing the organic solvents under vacuum conditions. The resultant dry lipid films on the inside wall of the round bottom flask were hydrated and dispersed with PBS. With the bath sonicatator and prob sonication, we have made small unilamellar transfersomes. Then synthetized transfersomes were evaluated to define their morphology, entrapment efficiency, and antimicrobial propertise.

Results: FA-Transfersomes had a particle size of about 350 nm and an entrapment efficiency of approximately 50%. The results showed that the zeta potential was negative. The minimum effective dose of the transfersomal formulation against Staphylococcus aurous was more than 300 Âµg/mL.

Conclusion: Nano-vesicles with their bilayer structures could pass through or merge with the outer membrane of the microorganism, which leads to the better drug delivery. In this study we showed that the encapsulation of FA may enhance its antibacterial effects against bacterial strains such as staphylococcus aurous. Our findings showed that an optimized FA-transfersome formulation could decrease the minimum inhibitory concentration of the drug and improve its efficacy against microbial pathogens.

Keywords: Nanocarrier, Transfersome, Ferulic acid, Skin, Nanomedicine

Treatment of cancer with chimeric antigen receptor (CAR) T cells. (Review)

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Introduction: Cancer means abnormal growth and proliferation of cells in the body. The incidence and mortality rate of this disease is increasing every year and causes serious problems in world health and public health. Factors such as mutations, cell cycle defects and damage to the DNA structure involve in cancer.

Methods: Has been stated that cancer can be treated if diagnosed early. Cancer by methods such as; Chemotherapy, radiation therapy, and the use of certain cancer drugs, such as hormonal drugs, can be treated. It is worth noting that surgery to remove cancerous masses was the first method that successfully used to treat cancer. As regards that many cancers resist treatment over time, recently has been shown that immune system, especially lymphocytes, involve in eradicating cancer.

Results: T cells are involved in cellular immunity, for example, the chimeric antigen receptor (CAR) T cells are considered in the treatment of cancer and malignancies. CARs consist of four main components: (1) a domain bound to the target antigen, (2) a hinge region, (3) a transmitting domain, and (4) one or more intracellular signaling domains. The chimeric antigen receptor (CAR) T cell is a recombinant receptor and a new treatment strategy that directly detects tumor and cancer antigens. When CAR T cells detect cancer cell antigens, are reproduced and kill them. CAR T cells are produced in a five-step process. First, T cells are isolated from cancer patients, then T cells are modified with CARs until T cells, in addition to identifying tumor cells, can produce CAR T cells. In the next step, under culture conditions, CAR T cells are cultured and the amount of these cells is increased by cytokines. Finally, the produced CAR T cells are injected into the patient at the appropriate dose. The process of producing CAR T cells takes about 3 weeks. These cells proliferate in vitro and are stored frozen for future use. Stimulating molecules such as CD28 can increase the antitumor activity of CAR T cells.

Conclusion: Currently, Patient and donor-derived CAR T cells are used to treat cancer patients. The most successful products are CAR T cells (tisagenlecleucel, axicabtagene ciloleucel, and brexucabtagene autoleucel), which target B-cell CD19 antigen and are an important treatment option for patients with acute B-cell lymphoblastic leukemia (B-ALL) or non-Hodgkin

lymphomas. Studies have shown that through CAR T cells, patients can live without the risk of recurrence.

Keywords: Cancer, chimeric antigen receptor (CAR), T cell

Using molecular dynamics simulation to explore the binding of the potent anticancer drugs sorafenib and streptozotocin, to functionalized carbon nanotubes (Research Paper)

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Introduction: Chemotherapy is a standard cancer treatment and scientists have proposed a variety of anticancer drugs for use in cancer treatment, but poor water solubility and serious adverse effects have limited the efficacies of many of those potent and promising drug molecules. These complications might be reduced by the use of a nanocarrier that targets the tumor site and only releases the drug at that site. Carbon nanotubes (CNTs) are among the most promising candidates for use as drug-delivery carriers. Carbon nanotubes (CNTs) are widely used in drug delivery systems (DDSs) due to their unique chemical and physical properties. Investigation of interactions between biomolecules and CNTs is an interesting and important subject in biological applications. In this study, Molecular Dynamics (MD) simulation is used to study the behavior of the anticancer drugs sorafenib (SF) and streptozotocin (STZ) on free and functionalized carbon nanotubes (FCNTs). The carbon nanotube has functionalized with valine or phenylalanine moieties to reduce their toxicity and increase their solubility in aqueous solutions

Methods: A series of MD simulations were carried out on different models to explore the interactions of anticancer drugs (SF, STZ) with carbon nanotubes. In all of the simulation model systems, an armchair single-walled carbon nanotube with a length of âˆ¼ 42 Ã… and a diameter of âˆ¼ 21 Ã… was used as the nanocarrier. The CNT model was generated using the TubeGen online server. In each FCNT, four functional groups were placed on the sidewalls of the nanotube. The GROMACS software package (version 4.5.4) with the CHARMM27 force field was used to perform all of the molecular dynamics simulations carried out in this work. A box of dimensions 6 Ã— 6 Ã— 6 nm was chosen for each of the systems, and the TIP3P water model was employed to fill the simulation box. The particle mesh Ewald (PME) method was used to describe long-range electrostatic interaction. The pressure (1 bar) and the temperature (310 K) were kept stable using the Berendsen algorithm and the Visual Molecular Dynamics (VMD) software was used to visualize the studied system.

Results: The influences of the positions and type of the functional groups present on the adsorption behavior of the anticancer drugs were investigated using molecular dynamics simulations. To verify the stability of the studied systems, the total energy, and the number of hydrogen were plotted. We can see that in each case the vdW energy dropped drastically and then fluctuated slightly until the end of the simulation. Thus, the vdW energy plays a significant role in the stability of the studied systems and the initial adsorption of the drugs. It is worth pointing out that the anticancer drug STZ has the lowest van der Waals energy with the CNT, with a value of ~ âˆ’248.87 kJ/mol. Note that

pristine CNT is not capable of forming hydrogen bonds, so no hydrogen bonds were observed between the drug molecules and the carbon atoms of a pristine nanotube. Analysis of the hydrogen bonds revealed that the numbers of drugâ€“functional group and drugâ€“water hydrogen bonds were greater for STZ than for SF. This behavior can be explained by the presence of several hydroxyl groups in the structure of STZ

Conclusion: The MD simulations revealed that functionalizing the CNT can affect the strength of the drugâ€“carrier interaction. It was found that the average van der Waals interaction energies between the drugs and FCNTs functionalized with valine were more negative than the corresponding energies when the FCNTs were functionalized with phenylalanine indicating that the van der Waals interaction energy between an anticancer drug and a FCNT can be affected by the positions of the functional groups on the CNT. Moreover, the drugs interacted more strongly with valine groups than with phenylalanine groups.

Keywords: anticancer drugs Molecular Dynamics (MD) simulation Carbon nanotubes