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Osmolytically Stabilization of Laccase and Lipase Under Harsh Conditions

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21-23 February 2023

Oral: O100

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Abstract:

Enzymes are highly complex systems and very sensitive, exhibiting substantial structural variability in their folded state under harsh conditions [1]. Osmolytes are known to play important roles in stress protection by stabilizing macromolecules and suppressing harmful effects on their functional activity [2]. They usually protect enzymes by the mechanisms such as increasing melting temperature and the unfolding free energy, offsetting the destabilizing effects of urea, and also inducing molecule folding [3]. Here, the effect of some osmolytes (betaine, mannitol, trehalose, sorbitol, and taurine) on the activity and stability of lipase and laccase was studied under ultrasound irritation, urea-containing, and thermal conditions. For this purpose, the conformational changes of the enzymes were analyzed by fluorescence spectroscopy, circular dichroism (CD), and differential scanning calorimeter (DSC). Furthermore, the kinetic parameters for the enzymes' activity as a function of osmolytes were studied in each environment-stress condition. Also, the stability of the enzymes in the presence of osmolytes was evaluated after storage in harsh circumstances. Betaine (1 M) improved the activity of laccase by 60% and its maximum velocity (V_{max}) by $436 \pm 0.8 \mu M$ at 60 °C. Moreover, betaine increased the melting temperature of the enzyme by 20 °C. Laccase was also protected by proline against urea denaturation in a concentration-dependent manner. As quantified by the CD spectra, sorbitol enhanced the rigidity of the lipase molecular conformational structure against the ultrasonic field. Under ultrasound irritation, fluorescence spectra of lipase in the presence of mannitol showed no shift in the emission maximum (λ_{max}) and little change in the fluorescence intensity. A decrease in fluorescence intensity of the enzyme after exposure to ultrasound might be the result of the reduction in the polarity of the tryptophan environment. Osmolytes act essential roles in stabilizing the secondary and tertiary conformations of laccase and lipase and maintaining their activity and stability under harsh conditions.

Keywords: Osmolyte; Laccase; Urea; Lipase; Thermal Stability; Ultrasound irritation.

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The Construction of a Novel Functionalized Hydroxyapatite Nanoparticles for Gene Delivery

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Abstract:

Gene therapy is the new generation of developing medical approaches which can target the cancer cells and return some lost functions. Hydroxyapatite nanoparticles (HANPs) are deemed feasible and possess many characteristics desired of a safe and effective gene vector. Herein we used a technique for synthesis a new factionalized HA particle in the nanometer range. The morphological and physicochemical properties of fine-tuning HANPs were investigated. Any other way, factionalized HA NPs due to its exclusive physicochemical properties are a good candidate for carrying of nucleic acids and can enhance transfection efficiencies of particles. Materials and methods: After construction and modification of HANPs with amino acid (Gly) and polyethylenimine (PEI), lyophilization were done. Characterization of the functionalized HA/Gly/PEI were done by FTIR, Zeta potential and SEM, too. Then cellular examinations were continued by gel retardation to investigation of DNA@HA/Gly/PEI NPs complex adsorption stability and MTT assay to make ensure to non-toxicity effect of the synthetic NPs. Results: As is evident from this result functionalized HANPs manifested a loading efficient nanoparticle in several ratio of functionalized HANPs to DNA. This situation was shown by Zeta potential data and gel retardation. In addition, MTT assay demonstrated moderate cytotoxicity in high concentration of HANPs. Discussion: In this study functionalized HANPs were synthesized as a biocompatible and biodegradable compound with suitable mobility and high surface area. The result of characterization showed the suitable properties of NPs for DNA loading. Therefor the evidence suggests the application of the factionalized HANPs as efficient approach for gene delivery. Conclusions: It was conducted that synthesized functionalized HANPs can be used as an efficient suicide gene delivery to the 2D and 3D cancer cell line models.

Keywords: Gene Therapy; Hydroxyapatite; Transfection; Nanoparticle.

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The High Potency of Laccase-Lipase Hybrid Nanostructures for Biodegradation of the Anthraquinone Reactive Blue Dye

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Abstract:

Hybrid nanostructures (HNSs) are defined as particularly conjugated organic and inorganic compounds, which represent higher functional potency than individual materials or even provoke new operations [1]. Among various types of HNSs, particles composed of enzymes as organic elements have been of great interest due to their extensive utilization, such as biosensors, nanomotors, and catalysts [2,3]. Laccase and lipase are the most known and applicable enzymes, which accept a wide range of substrates and catalyze synthesis and hydrolysis reactions, respectively; where co-immobilization of both enzymes reasonably extends their biocatalytic activities. Anthraquinone dyes, such as reactive blue (RB), are highly carcinogenic and mutagenic and also, because of their structural resonance and stability, are remarkably resistant to chemical oxidation [4]. Here, the hypothesis is that laccase/lipase-based HNSs can be utilized for the biodegradation of RB in an environmentally friendly approach without applying harmful chemicals or producing toxic byproducts. Experimental: Initially, a solution of copper sulphate was added into the sodium phosphate buffer pH 7.4 containing a catalytic amount of laccase, and then instantly a blue precipitate was formed, centrifuged, and washed three times with distilled water. In the next step, a solution of cobalt chloride was introduced to the former sediments suspended in the phosphate buffer pH 7.4 containing porcine pancreas lipase, subsequently, a purple precipitate was prepared and the washing process was repeated. The fabricated HNSs were assessed for reusability, thermal and pH, and long-term storage stability using associated substrates of 2,2'-azino-di (3-ethylbenzthiazoline sulfonic acid) (ABTS) and p-nitrophenyl palmitate (p-NPP) for laccase and lipase, respectively. After confirming the morphological properties of the structures with SEM, XRD, and TGA analyses, the HNSs were applied to study the biodegradation of a highly toxic anthraquinone dye. While the morphological analysis was in good agreement with the fabricated structures, in order to obtain HNSs with the highest biocatalytic activity, the effect of different variants, such as the concentrations of metal salts and phosphate buffers in each step was optimized using response surface methodology. With optimizing the conditions, the prepared HNSs represented a well-accepted biocatalytic activity, thermal and pH stability, long-term storage stability, and reusability compared to the free enzymes that emerged from the preservation of structural conformation due to the strict binding to the support and entrapment into the metal ions. Subsequently, the bio-removal percent of RB dye in the presence of HNSs was higher than the free enzymes, in which the surface adsorption in conjunction with the biodegradation is assumed as the route of elimination. This study offers a facile and instant approach to fabricating HNSs containing two different enzymes with high biocatalytic activity and unique features and therefore makes them a promising candidate for utilization in the biodegradation of anthraquinone dyes that existed in wastewaters.

Keywords: Hybrid nanostructures; Laccase; Lipase; Biodegradation; Reactive blue dye.

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Design and in-vitro evaluation of topical hydrogel containing resveratrol-loaded cationic nanocapsules

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Abstract:

Resveratrol (RSV) is a natural lipophilic phytoalexin that belongs to the stilbene family. Many studies have proven various therapeutic effects of trans-RSV. RSV can be utilized to ameliorate the appearance of lined, dry, creased, aged, or wizened skin. Numerous nanoscale drug delivery has been extensively investigated as a platform for RSV delivery, these particles have shown the capability of photostability, and increasing water solubility however low physical stability under UVA radiation and low drug capacity are the concerning issues. Nanocapsules are specific kinds of colloidal drug carriers, composed of two distinct compartments, an oily core surrounded by a polymeric wall. The present study aimed to develop a suitable nanostructure formulation for RSV topical delivery and assess the in-vitro characterization of nanocapsules. Materials and methods: RSV-loaded nanocapsules were synthesized by the nanoprecipitation method and characterized. The formulation was optimized using Design Expert software. Stability studies were conducted at 4°C and room temperature. Photostability was evaluated using a UV lamp and cabinet. The hydrogel of RSV-loaded nanocapsules was prepared and characterized. Ex vivo penetration/deposition study carried out using rat abdominal skin. Results: The nanoparticles had an average size of 166 ± 8.7 to 272.5 ± 12.5 with narrow size distribution, a zeta potential of 19.7 ± 6.3 to 37.6 ± 5.2 , and the EE was in the range of 69-99%. RSV-loaded nanocapsules were spherical, confirmed by Scanning Electron Microscopy. The optimized formulation exhibited high stability in size and EE with no signs of aggregation or creaming during the 90 days of storage at both room and 4°C temperatures. The photo-stability study revealed that 70% of RSV was retained in the formulation during 120 min of UV light exposure. The in vitro release study showed a sustained and slow-release pattern for 24 h. Compared to free drug hydrogel, a higher amount of RSV was achieved in viable layers associated with nanocapsules. Discussion: The optimized formulation had a particle size of 190 nm, and a zeta potential value of +32 mv with 95% entrapment efficiency. No creaming or aggregation was observed during the 90 days of the storage which can be a result of the high zeta potential which prevented the nanocapsule aggregation indicating high stability of 2 the formulation. A slow rate of drug release within the first hours and a prolonged release feature shows the retention of the drug in the nanocapsules and the total incorporation of RSV into nanocapsules. In our study after 24h, the epidermis and dermis layer were separated and the amount of RSV accumulated in each part was analyzed by HPLC. It was observed that a higher amount of RSV was achieved in the dermis layer when it was associated with nanocapsules. Conclusions: Thus, it can be concluded that prepared hydrogel of RSV-loaded nanocapsules has a high potential of delivering RSV in deeper layers resulting in dermatological benefits.

Keywords: Nanocapsules; Resveratrol; Eudragit®RS100; Photo-stability; Topical delivery.

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Injectable Photothermally Activated Hydrogel for Skin-Tumor Therapy and Multidrug-Resistant Infection-Induced Wound Healing

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Abstract:

Melanoma, with more than one million patients diagnosed yearly, results in significant morbidity and mortality. The conventional treatment process includes surgical excision followed by chemotherapy and radiotherapy [1]. However, the multidrug-resistant bacteria infected-wound and severe side effects of chemotherapy and radiotherapy are still important challenges. Therefore, there is a high demand for the development of novel multifunctional biomaterials that can simultaneously treat cancer and infected wounds for efficient skin regeneration. In recent years, photothermal therapy has made significant breakthroughs as a promising strategy to treat cancers and heal created wounds by hyperthermia [2, 3]. Copper oxide (CuO) is an attractive candidate as a photoactive agent, which can show combined antimicrobial and photothermal effects for regenerative applications [4]. Incorporating these nanoparticles along with regenerative drug molecules inside adhesive injectable hydrogels would allow the design of advanced formulations for skin-tumor therapy and tissue repair. **Materials & Methods** CuO nanosheets were synthesized by the precipitation method. Subsequently, PG hydrogel was prepared through the chemical crosslinking between poly (methyl vinyl ether maleic acid)-gelatin, followed by the incorporation of CuO and allantoin to form PGCA hydrogel. Physicochemical characterization, injectable property, and photothermal performance of the hydrogel were assessed. Furthermore, antibacterial activity, in vivo toxicity, wound healing assessment, and photothermal anti-cancer therapy of the hydrogel were evaluated. Results CuO nanosheets with lengths ranging from 100-400 nm were successfully synthesized. CuO nanosheets revealed good photothermal efficiency which could ablate cancer cells within 10 min at 1.5 W/cm² power density at the concentration of 400 µg/ml. Moreover, by exploiting the intrinsic properties of CuO and Alla, the hydrogel supported angiogenesis and proliferation of cells, respectively, which resulted in wound healing acceleration after cancer ablation. In addition, the abscess model results demonstrated that CuO could effectively kill bacteria owing to the synergistic effect of hyperthermia and inherent antibacterial properties. Finally, the histopathological evaluation of the principal organs of rats showed no organ damage, like necrosis and inflammation. **Conclusion** In this study, an injectable multifunctional hydrogel containing CuO and allantoin was prepared to ablate melanoma cells and bacteria simultaneously. Moreover, the hydrogel effectively promoted wound healing by stimulating fibroblast proliferation and enhancing angiogenesis.

Keywords: Photothermal therapy; Injectable hydrogel; Skin-tumor therapy; Wound healing; Antibacterial; CuO nanoparticles.

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A Biomimetic Cellulosic Porous and Biodegradable Scaffold with Antibacterial Properties for Bone Regeneration

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Abstract:

Bone-related diseases, such as cancers, infection, and trauma, are common clinical problems that result in hardly recoverable bone defects, which cause a burden to healthcare systems due to the prolonged hospitalization and long healing process. NIR-responsive scaffolds coated with photothermal agents can absorb near-infrared (NIR) light and convert it to thermal energy. The generated heat can be controlled to maintain the temperature of the defect site to 39-40 °C as it is approved to assist in enhancing the proliferation of human mesenchymal stem cells and promoting osteogenesis. In this study, mild heat-induced osteogenesis is studied by a biodegradable cellulose-based scaffold coated with Bismuth Sulfide nanoparticles (NPs) while its pores are filled with gelatin-hyaluronic acid thermo-responsive hydrogel. **Materials and Methods:** Bismuth Sulfide NPs were prepared using a simple chemical reaction and plant-derived cellulose scaffolds (C-scaffold) were coated with NPs entirely to generate Bi-scaffold. Then the scaffolds were immersed in gelatin-HA hydrogel for 4 hours (Bi-Gel scaffold). Following that, the scaffolds were dried by freeze-drying. Scanning electron microscope (SEM) was used to characterize the morphology and structure of the scaffolds. Elemental analysis, porosity, thermo-gravimetric analysis (TGA), and antibacterial activity of the NPs and scaffolds were evaluated. In addition, the mechanical properties of scaffolds, in vitro photothermal activity, and in vivo toxicity of Bismuth Sulfide NPs and scaffolds were assessed. **Results and Discussion:** Transmission electron microscopy (TEM) image shows that Bismuth Sulfide NPs have a uniform spherical shape with an average diameter of about 5 nm. The FE-SEM images of scaffolds demonstrated that the scaffold coated with NPs and impregnated with gel while indicating desirable porosity. The elemental analysis of Bi-scaffold confirms that the scaffold coated with bismuth sulfide sufficiently. The compressive strength of Bi-Gel scaffold is approximately about 17.2 MPa, which is much higher than trabecular bones (Mean value= 3.9 MPa). The photothermal performance of the Bi-scaffold showed that the temperature increased rapidly to 76°C after NIR laser irradiation at 1.5 W/cm², which confirms the high photothermal conversion efficiency of the scaffold. The scaffolds showed very potent antibacterial effect against *E. coli* and *S. aureus* under NIR irradiation. **Conclusion:** The Bismuth Sulfide coated cellulosic scaffold has great potential in orthopedic applications due to good NIR-mediated and hydrogel-assisted osteogenic performances and this study provide new insights into the design and fabrication of new-style osteoimplants for bone regeneration.

Keywords: Scaffold; Photothermal Therapy; Antibacterial; Bone Regeneration.

Reference:

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A Multifunctional Injectable Antibacterial Hydrogel for Photo/chemo/immuno Combination Therapy of Breast Cancer

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Abstract:

Introduction: Photothermal therapy (PTT) has attracted extensive attention in cancer therapy owing to the minimal damage to non-target tissues. Bi₂S₃ nanorods (NRs) are promising photothermal agents for cancer therapy due to their light-to-heat conversion ability to induce apoptosis in tumor cells. Combination of PTT with chemotherapy and immunotherapy has a high potential to increase the chance of cancer eradication without metastasis to other vital organs. In this work, cancer cell membrane (CCM) and sorafenib (SFN) were loaded into a photoactive injectable hydrogel to render tumor-specific immunotherapeutic function and chemotherapy to the prepared hydrogel. **Methods:** Bi₂S₃ NRs were prepared using a simple chemical reaction and coated with hyaluronic acid to form BiH NRs. An injectable hydrogel of poly methyl vinyl ether-maleic acid (PMVE-MA) and gelatin was prepared via chemical crosslinking. BiH NRs, CCM, and SFN, were loaded within the hydrogel. The physicochemical characterization and photothermal performance of the NRs and hydrogels were assessed. Afterward, the in vivo toxicity, the antibacterial activity of the hydrogels, and the anti-cancer effect were evaluated on a 4T1 tumor-bearing mouse model. **Results:** The rod shape nanoparticles, with an average particle size of about 57 nm were successfully loaded into the chemically crosslinked hydrogel, which had good injectability. BiH NRs demonstrated sufficient temperature elevation to kill cancer cells after 10 min of near-infrared (NIR) irradiation. No abnormality was observed in the histopathological analysis of the main organs of the treated groups. In addition, the BiH-loaded hydrogel showed very potent antibacterial activity. The combined intratumoral photo-chemo-immunotherapy demonstrated more anticancer effects than the individual photo-, chemo- or immunotherapy alone. **Conclusion:** In this study, an injectable hydrogel containing BiH NRs, CCM, and SFN is reported for cancer ablation via a synergistic effect. In addition, the injectable hydrogel had the capability to load drugs for sustained release in the cancer tissues over a long period.

Keywords: Injectable Hydrogel; Photothermal therapy; Chemotherapy; Immunotherapy; Breast cancer.

Reference:

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Preparation and Physicochemical Characterization of Novel Cu/Al-LDH Nanoparticle for Controlled Release of Ibuprofen

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Abstract:

The control of the drug release from drug carriers, embodying control of both the release rate of a drug and the delivery of this drug through suitable carriers (e.g., biocompatible, biodegradable with low or null toxicity), has been a major goal in drug delivery research over the last two decades. Synthetic inorganic materials with well-arranged voids and surfaces exhibit advantageous properties towards the solution of today's environmental and industrial problems and for the design of innovative composites for different front-line applications. As one class of inorganic nanoparticles, layered nanoparticles, especially the layered double hydroxides (LDH) also known very often as hydrotalcite-like systems or anionic clays, have attracted considerable interest as effective drug release systems since they can qualitatively resemble the conventional intercalation compounds [1]. The original discovered LDH was the mineral Hydrotalcite $[\text{Mg}_6\text{Al}_2(\text{OH})_{16}](\text{CO}_3) \cdot 4(\text{H}_2\text{O})$. In this regard, the name was given as hydro-talcite because of its water content (hydro) and also its resemblance to talc (talcite). It occurs usually in nature and also can be synthesized easily with other metal ions isomorphously substituted. One of the advantages of LDH among layered materials is the great number of possible compositions and metal-anion combinations that can be synthesized. Apart from that, has peculiar characteristics like good biocompatibility, high chemical stability, pH dependent solubility, etc [2]. Briefly, different amounts of $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$ and $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ with a natural ligand (including: acacia, honey and chitosan) were separately dissolved in 20 ml water/ethanol (1:1 ratio) solution as solvent by vigorous stirring. Following, solutions were homogeneously mixed; to increase the pH of the mixed solutions to 10, a sufficient amount of $\text{Na}(\text{OH})_2$ M solution, which acts as the precipitating agent added. Afterward, the mixed solution was exposed to microwaves [3]. Then, the drug added to the prepared formulation and mixed. The surface properties of the Cu/Al-LDH formulation such as shape and mean volume diameter evaluated. The percentage of the entrapment efficacy and release rate was also calculated. Results: In the present study, ibuprofen intercalated Cu/Al-LDH nano-hybrid were synthesized using the co-precipitation method. Using Honey as natural ligand showed the most favorable properties. XRD data and FTIR Spectroscopy of the intercalated nano-hybrid confirmed successful intercalation of Ibuprofen in the interlayer space of Cu/Al-LDH. Ibuprofen was loaded in the LDH formulation to the extent of 66.7 wt %. The release rate of the formulation also measured to be about 40% using a Franz cell. Results indicated that LDH formulation could be prepared using Cu, Al and natural ligands. This work also supports that Cu/Al-LDH nanoparticles can be an effective carrier for control and sustained release of Ibuprofen. In this regard, the advantages of using Ibuprofen intercalated LDH nanocarrier instead of bare drug on minimizing the adverse could be under investigation and show promising results.

Keywords: physicochemical properties; controlled release; Cu/Al-LDH nanoparticle; Natural ligands.

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An Injectable Metal-coordinated Multifunctional Hydrogel with Antibacterial Properties for Photothermal Therapy of Cancer and Wound

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Abstract:

Photothermal therapy (PTT), a promising noninvasive strategy, has intrigued emerging attention due to its widespread clinical applications. Also, activities to prevent the occurrence of second cancer like surgery and radiation therapy cause several side effects, affecting the overall health of patients. Therefore, an efficient new strategy is a high demand for promoted wound healing and cancer treatments. In recent decades, natural-based hydrogels exhibited attractive features in comparison to synthetic ones like biodegradability, biocompatibility, and higher water absorption capacity. Herein, we reported a PTT-assisted antibacterial system utilizing bismuth sulfide nanoparticles (BiH NPs) and allantoin (Alla) as a hydrophilic drug derived from plants, which could stimulate proliferation and cell migration for the acceleration of wound healing. So, the aim of this study is to use photothermal therapy as a local treatment strategy with minimal toxicity and high specificity in tumor cells is a promising approach for cancer ablation and wound healing acceleration. BiH synthesis was carried out through bismuth nitrate pentahydrate and thioacetamide reaction in an acidic environment. Gel-BiH-Alla hydrogel was prepared through abundant metal coordination among the functional groups of farsin gum and alginate via ferric ions. Physicochemical characterizations were performed to confirm the formation of the hydrogel. Furthermore, the injectability and rheology properties of hydrogels were assessed. The photothermal effect of the hydrogel was evaluated under near-infrared (NIR) light irradiation at 808 nm with a power density of 1 W/cm² for 10 min. Moreover, antibacterial activity and blood clotting tests were evaluated. Subsequently, in vivo wound healing and cancer phototherapy evaluations were carried out. The rod-shaped NPs, with an average particle size of about 57 nm, were synthesized and successfully loaded in the hydrogel. Gel formation assessment of hydrogel proved that without a crosslinker the hydrogel had fluidity. Scanning Electron Microscopy (SEM) results confirmed the porous structure of the hydrogel. In addition, the prepared hydrogel showed good injectability and self-healing capacity. The temperature of BiH-loaded hydrogel increased after NIR irradiation, which was efficient for wound healing and reduction of relative tumor volume in the breast cancer model. In addition, the hydrogel showed a desirable antibacterial activity due to the photothermal and bacterial killing effect of BiH and Alla. Moreover, the blood clotting test showed a significant decrease in hemostatic time and blood loss in hydrogel-treated groups in comparison to the control groups. In vivo wound healing study, demonstrated that wound area in the Gel-BiH-Alla group treated with NIR laser was the most efficient group in wound closure. The hematoxylin and eosin (H&E) staining results represented that Gel-BiH-Alla + NIR hydrogel treated wounds improved skin regeneration. In vivo cancer phototherapy results showed the relative tumor volume decreased in just Gel-BiH treated with NIR laser. Also, H&E staining proved that just in Gel-BiH + NIR group apoptotic cells were seen and the rate of angiogenesis was decreased in the referred sample. This novel multifunctional hydrogel demonstrated excellent hemostatic performance, antimicrobial activity, and photothermal-induced skin regeneration, which had great application potential in wound healing and cancer therapy.

Keywords: Multifunctional Biomaterials; Photothermal Therapy; Injectable Hydrogels; Cancer Thermotherapy; Wound Healing.

Reference:

Tao B, Lin C, Deng Y, Yuan Z, Shen X, Chen M, He Y, Peng Z, Hu Y, Cai K. Copper-nanoparticle-embedded hydrogel for killing bacteria and promoting wound healing with photothermal therapy. J Mater Chem B. 2019 Apr 21;7(15):2534-2548. doi: 10.1039/c8tb03272f.

Risk Assessment of Acrylamide in Different Baby Food Samples: Optimization and Validation Using Sensitive Microextraction Method and GC-MS

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21-23 February 2023

Oral: O109

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Abstract:

In April 2002, the presence of acrylamide in food was announced by the Swedish National Food Agency. First, its presence was detected in potato and grain-based products. The European Food Safety Authority (EFSA) has recently announced that based on animal and analytical studies conducted in 24 European countries and 6 food organizations, acrylamide can potentially increase the risk of cancer in consumers. Research has shown that the highest amount of exposure to acrylamide is through food, so it is predictable that the amount of exposure of children (based on body weight) to acrylamide is two to three times higher than that of adults. In this study, GC-MS device was used to analyze and determine the amount of acrylamide and then was evaluated the risk of carcinogenesis and non-carcinogenesis caused by its intake. Methods: In this research, a method for extracting and purifying of acrylamide using GC-MS was developed and validated. Then, the level of acrylamide was determined in 65 baby foods samples that were collected from the market in 2022. In addition, the non-carcinogenic risk (Target hazard quotient-THQ) and carcinogenic risk (incremental lifetime cancer risk-ILCR) and Margin of Exposure (MOE) of acrylamide intake through biscuit consumption were evaluated in children and adults. Results: For method validation, the parameters assessed were limit of detection (LOD) and limit of quantification (LOQ); the obtained values were 0.5 ng/kg, 1.65 ng/kg respectively. For quality control baby food samples spiked at level of 1 ppm were analyzed. The RSD% of QC samples were 8.75%. The results of this research showed that the mean concentration of acrylamide in baby food samples was 2231.576 ng/kg. The calculated CDI for acrylamide based on children's weight in the tested baby foods showed that the intake of acrylamide in babies aged 6-12 month was higher than in other groups. The THQ in babies under 6 month was in the safe range but babies 6-12 month and higher than 12 months were in non-carcinogenic risk. The highest level of ILCR was observed in babies 6-12 month. The lowest level of ILCR was observed in under 6-month babies. For acrylamide, the lowest benchmark dose confidence limits for the 10% benchmark response (BMDL10) were 0.43 mg/kg bw/day and 0.17 mg/kg bw/day, respectively, from experimental evidence. The results of MOE (0.17 and 0.43) showed that the risk of carcinogenesis was high in all age groups due to exposure to acrylamide. Conclusion: The results of this research showed that baby foods can be one of the sources of acrylamide intake by Iranian baby and all babies regardless of age may be at elevated carcinogenic risk.

Keywords: Gas Chromatography; Baby foods; Acrylamide; Iran; Risk Assessment; Mass Spectrometry.

Synthesis of GHK-Octanoic Acid Conjugate as A New Anti-Wrinkle Agent Using Solid-Phase Peptide Synthesis Method

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21-23 February 2023

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Abstract:

The human peptide GHK (glycyl-L-histidyl-L-lysine) is naturally found in human plasma, saliva and urine and its levels decrease with age. Such various effects of GHK peptide as anti-aging, anti-wrinkle, wound healing, anti-inflammatory, promotion of skin remodeling and collagen synthesis has been proven well via numerous in-vitro and in-vivo studies. Furthermore, this oligopeptide has showed a strong affinity for divalent copper (Cu²⁺) and GHK-Cu complex is also considered as an anti-aging agent. Despite the anti-aging effects of GHK and GHK-Cu, they cannot effectively permeate through the skin due to their hydrophilic natures. One of the best strategies for increasing epidermal delivery of the hydrophilic peptides is to conjugate them to the lipophilic moieties like fatty acids. We synthesized the previously reported GHK and GHK-palmitic acid and GHK-octanoic acid as a new derivative of GHK on Rink Amide resin. Fatty acids (3eq) were conjugated to the amino group of glycine in presence of HATU (0.3M) and DIPEA (1M). Kaiser test was used to qualitatively control the reaction progress at each step. These peptides were finally characterized using LC-Mass. All peptides were obtained with high yield and purity. The GHK-octanoic acid as a more permeable derivative of GHK was successfully synthesized with high purity.

Keywords: anti-aging; lipophilic moiety; solid phase peptide synthesis; Palmitic acid; Octanoic acid; epidermal delivery.

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Repositioning of FDA Approved Drugs Against Peripheral Cannabinoid Receptor 1 (CB1R) as Anti-Obesity and Treatment of Metabolic Disorder Using Computation and Molecular Modeling Study

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21-23 February 2023

Oral: O111

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Abstract:

The endocannabinoid system is very complex system that regulates different body functions, and also related to some metabolic disorders and obesity. Compounds with the inhibitory effect of CB1R (e.g., Rimonabant), which introduced in Europe and many others country as anti-obesity treatment (Acomplia) are usually associated to CNS adverse side effects. So, targeting CB1R with peripheral CB1R activity could be proposed as a valuable solution for metabolic and obesity disorders.

In this research, the most appropriate protein structure is extracted from the protein data bank (PDB id=5tgz). Based on the structure of potent CB1R antagonists, the pharmacophore model of CB1R antagonist activity was generated. The correctness of the desired pharmacophore model is evaluated which was followed by pharmacophore screening over FDA's chemical database. After, the successful compound which poses the pharmacophore criteria undergo through virtual screening with three level of precise in order to find the compounds with higher dock score over CB1R active site. The extracted compounds are ranked based on the obtained score and 20% of the highest scores are structurally classified and introduced. By assessing the calculated BBB and CNS penetration of the resulted compound, three compounds including itraconazole, remdesivir, and monoxerutin emerged with the ability of affecting over the peripheral CB1R.

The binding mode and their binding energy analyzed. Finally, the molecular dynamic behavior of the itraconazole with the lowest binding energy was compared with the rimonabant (as the internal standard for CB1R antagonist activity), which results in stable RMSD for over 20 ns which means like as rimonabant, itraconazole produced stable complex over the desired molecular target.

Keywords: Obesity; Metabolic disorder; Cannabinoid receptor antagonist; Virtual screening; Drug repositioning; Molecular dynamic simulation.

The Complete Sequencing of Leishmania Transcriptome and Mirnaome by Ngs Method

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21-23 February 2023

Oral: O112

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Abstract:

In the name of the ALLAH The complete sequencing of Leishmania transcriptome and miRNAome by the NGS method Introduction: Leishmaniasis is one of the most important skin and visceral infections in Iran. There is no vaccine for field prevention of this infection in the population at risk. The World Health Organization recommended that vaccine research was not useful for field study and that modified traditional methods (such as leishmanization) should be used to control the disease in at-risk populations. A Leishmania was isolated from agama agillis in Iran, which is not pathogenic for humans. This parasite can be a candidate for leishmanization and because its post-translational modification is similar to humans, it is useful for the expression of pharmaceutical proteins. For the use for leishmanization as well as the expression of recombinant proteins, there is not much information about its genomic sequence. The current project was designed and implemented to sequence the transcriptome and miRNAome of the Iranian lizard Leishmania. Materials and Methods: To determine the transcriptome and miRNAome of Leishmania promastigotes, they were cultured in RPMI1640 culture medium and when they reached the logarithmic phase, were separated by centrifugation. The promastigote RNA was extracted by standard method and determined the quantity and quality of RNA for sequencing in the laboratory of the Cellular and Molecular Biology Research Center of Shahid Beheshti University of Medical Sciences. The RNA sequencing was done with the Illumina PE machine by NGS Method. The raw data were received and reviewed and analyzed. Results: In this research, the number of 8316 mRNA, 83 tRNA, 63 rRNA, 83 ncRNA, 5 snRNA, 1039 snoRNA, 36 regions, 3 repeat region, 8343 CDS, 9597 Exon and 9292 Genes were detected in promastigote of Iranian lizard Leishmania parasite.

Keywords: Transcriptome; Leshmania; NGS; miRNAome

The Use of Collagen Plates "Farmadont Iii" In the Postoperative Period in Surgical Methods of Treatment of Gingival Recession

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21-23 February 2023

Oral: O113

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Abstract:

The problem of gum recession is quite relevant, since this pathology, depending on the degree of loss of periodontal attachment, provokes the development of complications that can ultimately lead to tooth loss. To eliminate this pathology, complex treatment is necessary, where the main stage is mucogingival surgery. About the main factor of successful healing is the sufficient production of collagen, which contributes to the regeneration of new tissue. One of the collagen-containing preparations is the sterile collagen plate "FARMADONT III". Currently, in the treatment of gingival recession, it is especially relevant to create conditions for successful healing in the postoperative period when performed surgical interventions, thanks to which the prognosis of recovery and regeneration of own tissues will be improved.

Keywords: collage gingival recession; connective tissue autograft; postoperative period; herbal biogenic stimulants; patchwork operations

The Experience of Using a Dna-Based Immunomodulator in The Complex Treatment of Patients with Moderate and Severe Exacerbation of Copd

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21-23 February 2023

Oral: O114

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Abstract:

Comparative study of the dynamics of clinical parameters and immune status of patients with COPD in the period of exacerbation when using Derinat as part of complex therapy. 58 patients with severe and moderate COPD exacerbation aged over 60 years who underwent inpatient treatment from April to November 2022 at the BSMU Clinic were examined. Men - 41 (71%), women - 17 (29%). The assessment of COPD exacerbation was carried out according to the parameters of the BODE scale. Immunological examination by enzyme immunoassay. In the first group (29 people), 1.5% r-r 5 ml of a solution of the immunomodulator sodium deoxyribonucleate (Derinat) was added to the standard therapy of COPD exacerbation in / m every other day No. 5, in the second group (29 people) – standard therapy without immunomodulatory therapy. All patients included in the study had a BODE index in the range from 4 to 9 points. At the same time, the index ranged from 4 to 6 points in 40 patients, and 7-9 points in 18 (among whom all were men), which indicates a possible unfavorable prognosis of the disease. According to the indicators of FEV1, the 6-minute walk test and the severity of respiratory symptoms (shortness of breath according to MRC), patients receiving immunocorrecting therapy with 1.5% solution sodium deoxyribonucleate (Derinat) 5 ml every other day as part of complex standard COPD therapy did not significantly differ from patients in the treatment of whom Derinat was not used. Under the influence of Derinate as part of standard COPD therapy, IL-6 and TNF- α indicators significantly decreased. The decrease in nitroblue tetrazolium blood test (NBT) as a result of treatment of COPD exacerbation confirmed the trigger role of bacterial pathogens in the genesis of COPD exacerbation. 1. During the study, no more significant changes in the indicators of FEV1, the 6-minute walk test were registered in patients with acute COPD, but respiratory symptoms (shortness of breath) had a more significant decrease. 2. The inclusion of the drug Derinat in the course of standard therapy of patients with exacerbation of moderate and severe COPD makes it possible to improve the indicators of humoral immunity, phagocytic activity and leads to a significant decrease in the early marker of the inflammatory reaction IL-6 and circulating immune complexes (CIC).

Keywords: COPD; BODE scale; immunocorrecting therapy; solution sodium deoxyribonucle; IL-6; nitroblue tetrazolium blood te

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The Effect of Chronic Stress on the Development of Vaccinated Myeloma Sp2/0 Ag14 in Balb/C Mice Against the Background of the Introduction of Sodium H

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21-23 February 2023

Oral: O115

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Abstract:

The effect of chronic stress on the development of vaccinated myeloma sp2/0 ag14 in balb/c mice against the background of the introduction of sodium humate from peat rashida kitapova, ksenia nazmieva, bulat gilmutdinov bashkir state medical university, ufa, russia the purpose of this study was to evaluate the development of myeloma sp 2/0 ag14 in linear balb/c mice under chronic stress against the background of administration of 5% sodium humate solution (GN). It was shown that chronic stress stimulates the development of vaccinated myeloma in BALB/c mice. When modeling stress against the background of the introduction of a 5% solution of GN, its inhibition occurs. The antistress effect of the 5% solution of GN was expressed in a decrease in the indicator of the "degree of depression". With simultaneous modeling of stress and administration of a 5% solution of GN, tumor growth was inhibited, expressed in a decrease in the volume of ascitic fluid to 55.3%, a decrease in body weight gain to 50.5%, an increase in median life expectancy to 76.7% and an increase in life expectancy to 58.3%. The results obtained can be used to prevent and improve the effectiveness of cancer treatment.

Keywords: Pharmacology; humat from peat; myeloma

Analysis of Bioethical Principles of Merchandising in Pharmacies of the Republic of Bashkortostan

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21-23 February 2023

Oral: O116

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Abstract:

Bioethics in pharmaceutical merchandising is a set of principles that prevent the negative consequences of modern sales technologies not only for the individual, but also for society as a whole. Bioethical issues in this case concern the problem of the possibility of interference with the physical and mental integrity of a person. Due to a number of features of the provision of pharmaceutical services in the pharmacy, it is necessary to modernize the merchandising tools, adapting them to the pharmacy organization. The relevance of this work is due to the need to study the bioethical principles of merchandising used by pharmacies in order to increase the level of trust and protection of visitors while increasing sales. The materials and methods of research were the content analysis of documents, publications on the Internet, the method of sociological research, the method of causal analysis of phenomena, the method of structural and functional analysis, and empirical research methods are also used: observation, description. The elements of merchandising are: a wide range, proper placement, presentation, advertising materials. All these elements have an impact on a persons consciousness, their improper use can harm the patient. Therefore, when using these elements in a pharmacy, it is necessary to adhere to the bioethical principles of merchandising – unobtrusiveness (reminiscent of advertising), honesty and openness of information, technology, timeliness. In order to analyze the bioethical principles of merchandising used in pharmacies of the Republic of Belarus, we conducted a pilot study of 65 pharmacy visitors. In general, respondents respond positively to advertising in the pharmacy 46.2%, but there are also those who react negatively 12.3%. 30.8% believe that advertising influences the respondents choice, 53.8% of respondents are not influenced by advertising. Many respondents pay attention to the attractive and convenient display of goods in the pharmacy. We analyzed the most memorable things in the design of storefronts for respondents: on the 1st place - the convenience of placing goods in the showcases, on the 2nd - the emphasis on low price, on the 3rd - the color scheme of the design of the storefronts, on the 4th - branded logos of drugs. When asked what kind of association is caused by the external design of storefronts, 35% noted concern for the population, 32% good quality of goods, 11% cost savings. More attractive discounts are: discount on discount cards 35%, bonus — accumulative program 30%, low price 23%. 33.8% would like to receive information about discounts and new pharmacy products via phone messages, 66.2% would like to receive messages by phone. The survey helped us to see the bioethical problems of using merchandising as an advertising technology for a pharmacy, to identify the preferences of customers and the points to which they pay attention while in the pharmacy and making a purchase, and also to understand that excessive advertising, such as phone alerts, rather irritates the buyer than attracts.

Keywords: pharmaceutical merchandising; bioethics; pharmacy research

Situational Assessment of the Range in The Segment of Off-Label Drugs

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21-23 February 2023

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Abstract:

The urgent need of drugs for the treatment of new infections that have flared up, as well as individual nosologies, pose vital and urgent unique tasks for the medical community to select effective pharmacotherapeutic treatment regimens in an extremely short time. The accumulated clinical experience shows that the use of a registered drug according to indications outside the instructions (off-label) is a potential way of such a targeted search. Previously conducted scientific research, including in 2016-2022 under the guidance of Professor Glembotskaya Galina, it has been proven that the re-profiling of drugs can significantly reduce the time and the total costs of pharmaceutical development. Within the framework of this study using the most well-known international databases, we conducted a targeted scientific and informational search and collected the evidence base of accumulated world experience in the field of re-profiling of medicines over the past 20 years. During the analysis, it was found that most of the drugs offered for reprofiling have identical originally registered indications for use. Based on this, the TOP 7 most common groups of drugs according to initial indications were identified, as well as the TOP 7 groups of indications for which the largest number of drugs were repurposed or considered for repurposing in the period under review. As a result of processing the data obtained, the most common according to the initial indications it turned out to be a re-profiling of antidepressants - 22.2% and antifungal drugs - 22.2%. Whereas the most common drugs according to the results of re-profiling are drugs for the treatment of oncological diseases - 22.0% and COVID'19 - 40%. In the development of the data obtained, we conducted a study of the economic feasibility of re-profiling the two most common groups of drugs in the field of repurposing at present.

Key words: off-label; re-profiling of drugs; repurposing

Audit and Inspection of Kazakhstan Pharmaceutical Companies for Compliance with the National Requirements

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21-23 February 2023

Oral: O118

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Abstract:

Any activity in the pharmaceutical field needs periodic external critical evaluation. Since the pharmaceutical industry has a direct impact on human quality of life and health, the evaluation of such activities should be carried out more thoroughly. It can be accomplished by means of several tools. The most common approach is self-evaluation (self-inspection, internal audit, first-party audit). Without these checks, other types of inspections are ineffective. Inspections/audits are an integral part quality management system. The aim of the research is to develop audit checklists for inspection and audit by the first party and to carry out evaluation activities of domestic pharmaceutical industries in compliance with the GMP and ISO requirements. Materials and methods. To conduct research various legislative documents were used: - Order of the Minister of Health of the Republic of Kazakhstan dated February 4, 2021 KP-ДЖМ-15 «On approval of good pharmaceutical practices» (Annex 3 GMP). - Order of the Minister of Health of the Republic of Kazakhstan dated January 27, 2021 KP-ДЖМ -9 «On approval of the rules of pharmaceutical inspections ». - ISO 19011:2011 «Guidelines for audit of management systems». - ISO 13485:2006 «Medical products». Inspection is planned at the LLP «Abdi Ibrahim Global Pharm» (Republic of Kazakhstan, Almaty) solid dosage form manufacturer. And also, the audit is planned at the LLP «DOSFARM» (Republic of Kazakhstan, Almaty) at the production site for the release of disinfectant solutions. Object of audit/inspection: quality management system of the enterprises; Audit/inspection topic: compliance with the requirements of the GMP, Order MoH RK KP-ДЖМ-15 «On approval of good pharmaceutical practices» Audit/inspection team: Bekbolatova E.N. - Chief Auditor/Inspector, auditors/inspectors - Malgazhdarova A.A., Matzhan A.B.; Audit day: February 1 and 2, 2023. Research findings. Plans for inspection / audit of the quality management system of the local manufacturing sites were developed within the framework of the annual plan of enterprises for inspection and audit. The algorithm of the audit was created. Preparatory work includes: training of internal auditors/inspectors, establishment of a list of internal auditors/inspectors, appointment of a chief auditor/inspector, collection of an auditor/inspection file. Main activities: preparation of the plan, development, approval and distribution of the Audit/Inspection Programme and Checklist, preparation for the inspection/audit, audit/inspection (introductory meeting, audit/inspection itself, closing meeting), preparation of the audit/inspection report, evaluation of the group's work, development of corrective/preventive actions (CAPA), verification of the CAPA performance (next scheduled audit or out-of-scope audit), creation of audit dossier. As part of the audit and inspection, checklists have been developed in accordance with national standards, as well as successfully conducted the audit / inspection of the enterprises, verified the elimination of CAPA comments from previous audits / inspections. Findings. Thus, research work on audit/inspection of local pharmaceutical enterprises have been successful, which confirms compliance of quality assurance department with national requirements of legislation.

Keywords: Audit; Inspection; NATIONAL REQUIREMENTS.; Kazakhstan

In-Silico and In-Vitro Investigation on the Antibacterial Effects of the Methanol Extract of *Chenopodium album* L. on Five Gram-Negative Bacteria.

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Abstract:

The rise in bacterial drug resistance, which raises patient expenditures and mortality rates, is one of the most significant concerns facing humanity today. Nature has always presented us with solutions to these problems. Plant extracts are intelligent combination of various active compounds. Plant extracts can exert additional antibacterial effects via many routes, therefore there is a possibility that they will reduce the emergence of new antibiotic resistance. *Chenopodium album* L. (CA) is an annual Asteraceae shrub used as an anti-inflammatory and hepatoprotective drug in traditional medicine. We obtained CA highly polar active chemicals from the IMPPAT, KNAPSAcK Core System, Dr. Dukes Phytochemical and Ethnobotanical, and SwissADMET Online Databases for this investigation. Then, we utilized the Path2Way platform to calculate the potential effects on different microorganisms. Cytoscape 3.9.1 exhibited the network activity of various CA compounds and bacteria. To validate the In-Silico findings, CA was extracted with 80% methanol from the Alborz province. Then, we conduct CLSI-based Zone of Inhibition Diameter, MIC, and MBC testing on five gram-negative bacteria. The examination of databases yielded 63 chemicals, 44 of which were very polar. It was projected that 26 polar chemicals would have an effect on bacteria; Betaine and Vanillic acid are the most potent. The five most affected microorganisms are *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella enterica*, *Klebsiella pneumoniae*, and *S. typhimurium*. The results of the Zone of Inhibition indicate that CA is efficient against *E. coli*, *P. aeruginosa*, and *S. typhimurium*. The optimal MIC for *E. coli* and *P. aeruginosa* was 62.5 mg/mL, while the MBC findings were similar for all five organisms. By comparing the outcomes of In-Silico and In-Vivo trials, it appears that although betaine has the highest impact likelihood on *P. aeruginosa*, *K. pneumoniae*, and *S. enterica*, its quantity in our CA methanolic extract is too low to have an effect on two of these bacteria. Due to the positive results on *P. aeruginosa*, it appears that the levels of Chenoalbuside, Rutin, and 3,6,9-Trihydroxy-4-megastigmine in this extract are potentially significant. In addition, for the purpose of predicting the extract content, these trials indicated that CA is an effective bacteriostatic agent against *P. aeruginosa*, one of the most troublesome organisms in public health regions.

Keywords: *Chenopodium album*; Antibacterial; Bioinformatics; *Pseudomonas aeruginosa*.

Reference:

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Study of the Effect of Oxytocin on the mGluR1 and mGluR5 Glutamate Receptors on Valproic Acid Induced Autism in Male Rats

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21-23 February 2023

Oral: O120

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Abstract:

Autism is a type of developmental disorder that is characterized by abnormal communication and verbal behaviors and appears in the first years of life. This disorder affects the normal development of the brain in the area of social interactions and communication skills. Autism is seen 3-4 times more in boys than in girls. So far, there is no successful drug treatment for this disease [1]. In recent studies, it has been reported that children who received oxytocin showed significant improvements in behavioral, emotional and social problems compared to other affected children. Behavioral improvements associated with oxytocin treatment are related to changes in brain signaling. If the effect of oxytocin can be effective on these patients, then the receptors that can be affected by oxytocin can also be specially investigated as one of the study goals. In this research, we are looking for the effect of oxytocin on mGluR1, mGluR5 receptors and finally the relationship of this effect on the induced model of autism with valproic acid in male rats. In this study, male and female Wistar rats weighing 200 to 250 grams were used. Day and night lighting was 12-12 and access to water and food was ad libitum. Fertility cycle of these mice was controlled and their ovulation date, male and female mice were placed next to each other to mate. Then, the vaginal secretions of Syrian mice were collected and spermatozoa were seen under the microscope to confirm successful mating, and the pregnancy of Syrian mice was confirmed on the first day. Pregnant mice were separated and divided into two groups. In the first group, on the 12th day of pregnancy, Valproic acid was administered in a single dose of 500mg/kg i.p. and [2] in the second group or the control group, on the 12th day of pregnancy, only normal saline was administered to pregnant mice by i.p. was injected Male infants born from both groups of mothers were examined for autism using Marble burying self-grooming and Barnes Maze behavioral tests. After confirming autism, male infants born who were diagnosed with autism and male infants born of the control group were injected with oxytocin in a single dose at 21 days of age with a concentration of 200 µg/kg i.p., just before performing behavioral tests [3]. After performing these tests, molecular Western blotting and ELISA tests were performed on the brain tissues from the amygdala and hippocampus regions of the investigated mice, separated and analyzed. The effect of Oxytocin in the autism induced model with valproic acid led to a positive improvement in correcting behavior, reducing errors and improving spatial memory. This can be related to the decrease in glutamate concentration and the decrease in the expression of mGluR5 and mGluR1 receptors in the amygdala and hippocampus. Considering the use of oxytocin as a medicinal combination, it seems that this combination can be a suitable candidate for the treatment of autism disorder by improving the behavioral, emotional and social problems of patients.

Keywords: mGluR5; mGluR1; oxytocin; autism

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Evaluating The Efficacy of Alcohol and Chlorhexidine-Based Disinfectants Against Drug Resistance *Acinetobacter* Spp. Isolated from Patients in the ICU

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21-23 February 2023

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Abstract:

Since the 1970s, the prevalence of hospital-acquired infections has been increasing rapidly worldwide. Disinfectants play an important role in controlling and preventing the spread of infection in hospitals. Especially the spread of drug-resistant *Acinetobacter* strains has caused many concerns. Considering the established drug resistance, it is important to ensure the effectiveness of disinfectants, especially in cases related to hospital infections. Our aim in this research is to investigate the effect of two commonly used disinfectants, 70% alcohol and chlorhexidine, on drug-resistance strains of *Acinetobacter baumannii*, isolated from patients in the ICU department of Imam Hossein hospital. Thirty clinical samples were evaluated in order to identify *Acinetobacter* using TSI, SIM, SC and liquid urea (U) differential culture media. the susceptibility of the species to antibiotics was determined by E-Test method and disk diffusion method. MIC and MBC of the disinfectants were determined and after validating the neutralization method of disinfectants, the lethality of disinfectants was investigated at 15, 30 seconds and 1, 2, 5, and 10 minutes. Results: All 30 strains identified as *Acinetobacter* were resistant to amikacin, ampicillin-sulbactam, levofloxacin and meropenem. Only 3(10%) strains were sensitive to colistin. MIC and MBC of 70% alcohol (except for 1 strain) were in the range of 2.5%-10% V/V and in the range of 10%-40% V/V, respectively. MIC and MBC of chlorhexidine were in the range of 20-80 mg/l and in the range of 20-320 mg/l, respectively. 70% alcohol was able to destroy 100% of the strains after 10 minutes. While, chlorhexidine eliminated 100% of the strains with the following situations: 0.2% chlorhexidine after 1 minute, 2% chlorhexidine after 30 seconds 4% chlorhexidine after 15 seconds. Alcohol-based solutions, especially hand sanitizers, are widely used as antiseptic and disinfectant in clinical environments. The results of the present study show that 70% alcohol is ineffective against resistant strains of *Acinetobacter* in the times determined by health protocols (15-30 seconds) but 2% and 4% chlorhexidine were able to destroy all the investigated strains after 30 seconds. Therefore, widespread use of alcohol-based disinfectant and antiseptics in clinical environments especially hospitals should be seriously reconsidered. Chlorhexidine can be a suitable replacement against resistance strains.

Keywords: Antibiotics susceptibility; Drug-resistance *Acinetobacter*; Disinfectants; Antiseptics, E-test.

Development of Methods of Chemical and Toxicological Analysis of Pregabalin

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21-23 February 2023

Oral: O122

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Abstract:

Pregabalin is an analogue of gamma-aminobutyric acid (GABA), which has an analgesic and anticonvulsant effect. The literature describes a number of cases of abuse of pregabalin with the subsequent formation of dependence on it. The euphoric effect of pregabalin in patients abusing sedatives (including alcohol) was noted even before the release of this drug on the pharmaceutical market and confirmed by studying the addictive activity of pregabalin. In the practice of forensic examinations, there are no reliable methods for isolating and detecting pregabalin. In this regard, there is an urgent problem of developing methods of chemical and toxicological analysis in pregabalin poisoning. In the course of our research, we modified the method of isolating pregabalin from biological material according to the method of A. A. Vasilyeva and Stas-Otto. Factors affecting the release of the studied substance from the object are taken into account. When pregabalin was extracted with a mixture of chloroform-n-butanol (9:1) in an alkaline medium (pH 9-10), the yield of the substance was 74.96%. A thin-layer chromatography technique has been developed in a solvent system of 96% ethanol-isopropanol-25% ammonium hydroxide solution (20:10:0.5) to identify the toxicant. A solution of ninhydrin in n-butanol was used as a detecting agent. For the confirmatory analysis, we further developed the TLC-IR spectroscopy technique. In the detection method using IR spectroscopy, the analyte was preliminarily purified by thin-layer chromatography. As a result of the analysis, the structure of the analyte under study was confirmed in comparison with the working standard sample. When interpreting the results obtained, characteristic absorption zones are visible at 1417.84; 1448.04; 1388.82; 1368.82 cm⁻¹, characteristic of valence vibrations of C-H, C-H₂ and C-H₃ groups. The valence vibrations of the NH₂ group with an absorption band of 2266.84 cm⁻¹ are located in the high-frequency zone, and the C=O group gives spectra at a wavelength of 2956.08 cm⁻¹. The developed methods can be used for the purpose of chemical-toxicological, forensic analysis and for the diagnosis of acute poisoning with pregabalin in the practice of forensic chemical examination.

Keywords: Pregabalin; poisoning; isolation; thin-layer chromatography; IR-spectroscopy

References:

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Pharmaceutical Market Evaluation of Solid Dosage Forms (Tablets) on The Basis of the Wormwood in The Territory of the Republic of Kazakhstan

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21-23 February 2023

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Abstract:

Pharmaceutical market analysis of medicines in the form of tablets registered in the territory of the Republic of Kazakhstan (RK) containing the herbal medicine wormwood. Materials and Methods. The following database was used for the analysis of the pharmaceutical market: The state register of medicines and medical devices registered in the Republic of Kazakhstan. Results. 7461 brand names of medicines are registered on the market of the Republic of Kazakhstan. The largest share of which are tablets (41.52%). This trend is due to the widespread use of this dosage form, as ease of use, accuracy of dosage, as well as stability over time in different packaging material. Tablets are used to treat diseases in the following areas: Cardiovascular system (25%), antimicrobials (15%), nervous system (13%), digestive tract (12%), respiratory organs (8%) and genitourinary organs and sex hormones (7%), etc. Registered tablets represent 57 countries, 11.8% are domestic manufacturers (Top Five: Nobel Almaty Pharmaceutical Factory - 47%, Abdi-Ibrahim Global Pharm 14%, JSC Santo 13%, Viva Pharm - 12%, LLP TC Pharm Aktobe - 4%), 88.2% - foreign (Top Five: Republic of India - 19%, Federal Republic of Germany and Republic of Turkey 8% each, Russian Federation - 7%, Republic of Slovenia - 5%). It should be noted that tablet dosage forms in the market are mainly film-coated tablets (61.5%), conventional tablets (29.1%) are also widely used, more than 4% tablets are for absorption, dispersion and chewing, more than 3% are sublingual tablets and effervescent tablets. Only two wormwood medicines in the form of tablets are registered on the territory of the Republic of Kazakhstan, the first under the trade name "Antipollin wormwood", produced by the domestic manufacturer "Burli" LLP and the second "Norvela" - manufacturer "Dong-A ST Co., Ltd.", Republic of Korea. The first drug is presented in the form of tablets for absorption, they are used for allergen-specific immunotherapy in adults, children, adolescents aged 5-60 years with seasonal pollinosis with clinical manifestations of allergic rhinitis, allergic conjunctivitis, urticaria, bronchial asthma, bronchitis in patients with hypersensitivity to wormwood pollen. A herbal substance extract from the pollen allergen of wormwood was used as the active ingredient. The second drug is used for the treatment of diseases associated with disturbed acid production, damage to the gastric mucosa (erosions, hemorrhages, hyperemia, edema) in acute and chronic gastritis. Herbal plant wormwood (*Artemisia serotina* Bunge) presents the scientific and practical interest, as it is assumed to have wide pharmacological activity and is a potential active herbal substance. Conclusion. Overall, tablets are the optimal dosage form among oral medicines. Kazakhstan market is significantly dependent on imports, which can be reduced by expanding domestic herbal preparations.

Keywords: Tablets; Analysis of market; Pharmacy; Artemisi

Evaluation of Efficacy of Mouthwash and Oral Tablet of Propolis on Prevention and Treatment of Mucositis in Patients Undergoing Bone Marrow Transplant

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21-23 February 2023

Oral: O124

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Abstract:

Mucositis, including acute toxicities, is common, dose-dependent, and debilitating in patients undergoing chemotherapy, radiation therapy, and undergoing bone marrow transplantation. Occurrence of mucositis can limit the treatment process, change in protocol, difficulty in swallowing, change in taste, occurrence of dry mouth, weight loss, nausea and vomiting, pain, burning and heaviness of the stomach, occurrence of bloating, local and systemic infections, increase duration of hospitalization and costs and the reduction of the patient's quality of life. This study aimed to evaluate the effectiveness of mouthwash and oral propolis tablets on mucositis in patients undergoing bone marrow transplantation. Methods: 75 patients were included in a three-blind randomized study with placebo, 36 people were in the drug group and 39 people were in the placebo group. Patients gargled 5 ml of mouthwash for 30 seconds twice a day and then spit it out. Oral tablets were also given to the patient every 8 hours. The degree of oral mucositis was determined based on the grading criteria of the World Health Organization. Gastrointestinal mucositis was also investigated by considering factors such as the degree of nausea, vomiting, loss of appetite, pain, burning and heaviness of the stomach and flatulence. Results: Taking oral tablets and propolis mouthwash, compared to placebo, reduces the severity and duration of mucositis, delays its occurrence, reduces pain intensity, dysphagia severity, the number of days requiring total intravenous nutrition and the need for non-narcotic painkillers and shortens the time was hospitalized (P-value < 0.05). This drug had no effect on the sense of taste, dry mouth, need for narcotic painkillers, the result of blood culture after transplantation, the number of days of fever, the patients need for total intravenous nutrition, the time of transplantation of white blood cells and platelets (P-value > 0.05). One of the possible side effects of propolis is nausea, vomiting (6 patients) and skin rash (a patient). Conclusion: It is recommended to use propolis mouthwash and oral tablets to reduce the severity of mucositis in bone marrow transplant patients, as well as to design more studies by examining the effectiveness of different doses and other forms of propolis.

Keywords: Oral mucositis; Gastrointestinal mucositis; propolis mouthwash; propolis tablets; bone marrow transplantation

Preparation, Physicochemical Evaluation and in Vitro Kinetic Release Study Profile of Fluconazole Niosomes

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21-23 February 2023

Oral: O125

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Abstract:

Fluconazole is an antifungal drug that is effective against a variety of pathogenic fungi. Topical fluconazole is recommended for treating skin infections [1]. For topical delivery, sustained drug release, cutaneous accumulation for localized effects in different layers of skin, and a low level of penetration into the systemic circulation would be advantageous features. Niosomes, as an important class of lipid-based vesicular systems, with unique benefits, have attracted much attention as the high-potential drug delivery carriers over the past 35 years [2]. In this research, we prepared and studied fluconazole niosomes potential for topical delivery. Materials and methods: Film hydration as preparation methods; Span 20, 40, and 60, and their water-soluble derivatives (Tween 20, 40, and 60) and cholesterol were used for the preparation of niosomes. The shape of niosomes, mean volume diameters, and physical stability was evaluated. Encapsulation efficiency percent was calculated. Different kinetic models, including zero order, first order, Higuchi, Peppas, and Hixson-Crowell were assessed to determine the best kinetic model for releasing fluconazole niosomes. Results: Multilamellar vesicles are formed by all surfactant and cholesterol combinations. For many niosomal formulations, single-mode size distribution, good encapsulation efficiency (over 50%), were observed. Niosomes had high physical stability during 6 months' storage at refrigerator temperature. Selected formulation released 65 % of drug during 4 h. Discussion: The best model fitted with release data from selected formulation was Higuchi ($R^2 = 0.9653$ and $K = 3.36$), which showed the prominent diffusion mechanism of fluconazole through lipid bilayers [3]. Conclusions: Results of this study indicated that Span/Tween/cholesterol mixtures could form stable fluconazole niosomes. The results were promising for further topical in vivo applications of fluconazole niosomes in various fungal infections.

Keywords: Fluconazole; Niosome; Release profile; Physicochemical

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Cost-Effectiveness Analysis of Dapagliflozin in The Management of Heart Failure with Reduced Ejection Fraction (Hfref): A Systematic Review

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21-23 February 2023

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Abstract:

This study aimed to systematically review published economic studies to determine whether dapagliflozin, a sodium-glucose co-transporter inhibitor, plus standard care therapy (SCT) is cost-effective in heart failure with reduced ejection fraction (HFrEF). Method: We searched relevant keywords in PubMed, Scopus, Web of science, and Google Scholar to find related articles. Costs, QALYs, and ICERs were extracted from eligible studies. Results: Ten studies were finally included in the systematic review. The results of the quality assessment of the study showed a reasonable quality of all studies. Incremental QALYs were in favor of the dapagliflozin plus SCT treatment regimen. In all the studies, the incremental costs per QALY were below the willingness-to-pay (WTP) threshold with the exception of one study in the United Kingdom which the ICER and WTP were \$83,650 and \$50,000. All the studies determined the National Health Care perspective. The highest and lowest ICERs were \$83,650 and \$1991 per QALY in the United Kingdom and Thailand, respectively. Results of cost-effectiveness analyses showed that adjunct dapagliflozin plus SCT is cost-effective compared to SCT alone despite the additional costs of the drug. Finally, it can be concluded that dapagliflozin is a worldwide cost-effective adjunct medicine in HFrEF management.

Keywords: Dapagliflozin; heart failure; cost-effectiveness

Challenges and Opportunities for Import Substitution of Pharmaceutical Products Packaging Items in Iran

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Abstract:

Import substitution is the replacement of imported products with similar domestic products. In fact, the purpose of this strategy is to increase the growth and prosperity and improvement of the domestic industry, as well as to increase job creation and finally to reduce the dependence on other countries in the applied field. Considering the importance of packaging items in the production of pharmaceutical products, the present study was aimed to investigate the challenges and opportunities of applying the import substitution strategy in the field of pharmaceutical packaging items. Methods In this qualitative study, data collection was done by semi-structured interview method. The interviews were performed in-person. In order to increase the validity of the results, data was collected based on triangulation approach; that is both the companies producing packaging items and the companies producing pharmaceutical products were included. For data analysis, content analysis method was used using MAXQDA software. Results A total of 18 companies producing pharmaceutical products and 7 companies producing pharmaceutical packaging items were included in the study. The 27 respondents' (18 male and 9 female) job positions included: business manager, sales manager, sales expert, human resources manager, chairman of the board, etc. The mentioned challenges included financial and economic issues (the high price of domestically produced products due to the lack of preferential currency allocation, preferential currency allocation to imports, banking problems, fluctuations in exchange rate and price), inappropriate pricing of domestic products, difficulties of foreign payments, political issues including sanction, challenges caused by inappropriate policies and laws (difficulties in exporting, inappropriate policies and lack of adequate/appropriate support and trustee, legal-administrative processes), domestic production deficiencies (weakness in quality, insufficient quantity, difficulty in supplying raw materials, lack of technology or other necessary facilities in some cases, weakness in packaging design and introduction of products), other problems including monopoly/low competition, failure to address the problems of producers, some types of corruption, high cost and low efficiency of human resources, lack of inter-organizational coordination. The identified opportunities included the opportunities arising from the characteristics of the pharmaceutical packaging industry (uncomplicated nature of these items, the presence of many related technologies, the increase in the number of domestic manufacturers, the characteristics of the pharmaceutical industry, access to petrochemical resources within the country), the increase of the currency exchange rate, policies and political issues (country leader's slogans, protective policy-high import tariff, protective policy-import ban and conditions caused by sanctions). Conclusion According to the findings, the use of import substitution is not a negative point in itself, but there are many factors and challenges to achieve success by this policy that must be taken into account. Currently, in Iran, in the field of packaging items, in some cases this strategy has been successful and, in some cases, it needs more attention. In general, it seems that the quality of the domestically produced packaging products extremely differs product by product. It is also important that consider which countries have been considered as the comparators to address quality.

Key words: Import substitution; Pharmaceutical industry; Packaging; Developing country

Intravenous Human Immunoglobulin Utilization Patterns in a Middle Eastern Teaching Hospital

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21-23 February 2023

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Abstract:

Drug use evaluation helps to investigate and modify the pattern of drug administration with the aim of improving patient care and cost saving. Considering the important indications of intravenous immunoglobulin (IVIG) and its high cost, assessment of its prescription pattern could be helpful to increase the health system efficiency. Objectives: This study was aimed to investigate the IVIG pattern of use in a tertiary teaching hospital. Methods: This retrospective study included all in patients who received IVIG over spring and summer 2020. The needed information was extracted from patients files. Data were analyzed using SPSS software and compared with the standard guidelines. The study protocol was approved by the Ethics Committee of Hamadan University of Medical Sciences. Results: 72 patients received IVIG. The indications were "FDA-approved" and "CEDIT-acknowledged" for 33.3% and 61.1% of the cases, in order, and 45.8% adhered to the "red" indications of the UK protocol. Also, all prescriptions were in accordance with the approved indications of the FDO guideline. Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy, and COVID-19 were the three most common causes of IVIG administration. 66.7% had received the recommended dosage regimen and 51.3% experienced drug side effects requiring some measures. Conclusion: The occurrence of adverse drug reactions in more than half of the studied patients and related costs substantiate the need for enhancing physicians' refrain from unnecessary prescription of the IVIG, nursing staff's knowledge, and the inclusion of a clinical pharmacist in the healthcare team.

Keywords: IVIG; Immune globulin; DUE; Drug use evaluation; Rational prescription

Antiradical Synergy of Chlorogenic and Caffeic Acids with Glutathione

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21-23 February 2023

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Abstract:

Antiradical synergy of chlorogenic and caffeic acids with glutathione Introduction: Chlorogenic and caffeic acids (its main metabolite) are known for their numerous therapeutic effects, in particular, antioxidant activity [1–3]. Being natural compounds, they are often found in foods and dietary supplements. In living organisms they may interact with another natural antioxidant – glutathione. The copresence of these antioxidants in one mixture may result in an antagonistic or synergistic antiradical interaction between the components [4,5]. The result of this interaction at different ratios of components was the purpose of our study. The spectrophotometric ABTS/PP lag-time approach was employed to assess the antiradical activity of the compositions at different ratios in vitro [6,7]. The chlorogenic acid – glutathione and caffeic acid – glutathione binary mixtures with ratios from 1:5 to 1:20 were assessed. All the compositions demonstrated synergistic effects. The maximum synergy of 109% for caffeic acid and glutathione compositions was observed at the ratio 1:5. Chlorogenic acid with glutathione showed more considerable synergy up to 127% at ratio 1:5. Chlorogenic and caffeic acids in compositions with glutathione demonstrate considerable antioxidant synergy in vitro.

Keywords: Antioxidant activity; Caffeic acid; Chlorogenic acid; ABTS radical cation; Kinetic behavior

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Changes in Hemostasis in Pregnant Women with COVID-19

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21-23 February 2023

Poster: P104

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Abstract:

The severity of COVID-19 has a direct correlation with perinatal outcomes; the earlier and more severe the infection, the poorer the outcome for the fetus [2,6,10]. Due to insufficient data on the pathomorphological mechanisms affecting the maternal-placental-fetal system, NCVR poses unanswered questions to the medical community. The study was conducted on the basis of the maternity department of an infectious diseases hospital and was aimed at studying retrospective data to identify the features of the course of pregnancy, laboratory changes and histological studies of the placenta against the background of COVID-19 manifestation. Pregnant women hospitalized in the specialized department of an infectious diseases hospital for the treatment of patients with coronavirus infection were included in the study. Inclusion criteria were: singleton pregnancy, infection with COVID at 28 weeks or more, availability of voluntary informed consent for the study. We divided pregnant women into two groups according to the treatment prescribed: pregnant women who were prescribed low-molecular-weight heparins to prevent thrombotic events (n=87) and the second group: pregnant women who were not prescribed low-molecular-weight heparin (LMWH) therapy (n=69). According to the guidelines for organizing medical care for pregnant women, women in labor, delivery, and newborns during new coronavirus infection COVID-19 (version 1, dated April 24, 2020), it was recommended that therapy regimens for patients with severe infection include low-molecular-weight heparin preparations, which does not regulate the mandatory prescription of LMWH for patients with medium and mild degrees of severity of the infection. Both groups were comparable in age and height. Prevention of thrombotic events by administration of low-molecular-weight heparins (mainly enoxaparin sodium) was indicated for group I pregnant women. Due to the significant number of patients with pneumonia, and hence decreased respiratory function of the lungs due to inflammation and interstitial edema, pregnant women required oxygen support (24.6%). However, it was found that the need for oxygen therapy was statistically significantly higher in Group II patients, where the infection initially had a milder degree of NCDI.

Keywords: pregnancy complications; New Coronavirus COVID-19; pregnancy; hemostasis system; perinatal outcomes

Regulatory Changes in The Rules of Medicines Circulation within the Eurasian Economic Union

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21-23 February 2023

Poster: P105

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Abstract

The aim of the work is to conduct a content analysis of the main changes in the rules for registration and examination of medicines within the Eurasian Economic Union and to identify their specific features. It shows liberalization of registration and expertise procedures, increased availability of some unregistered medicines, changes in the terms of registration and expertise towards reduction. Certain inaccuracies in the changes to the rules have been established.

Keywords: Eurasian Economic Union, medicines circulation, registration of medicines

The Role of Presynaptic Modulation of Dopaminergic Pathways in The Brain in Therapy of Psychiatric Disorders

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Poster: P106

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Abstract:

Nowadays, the arising problem of the increase of the severity of the consequences of psychiatric disorders may seem overwhelming. In addition, there is a clear escalation in the number of reported cases of admission of the patients to the psychiatric wards. This alarming tendency led to the increased interest in studies of the functions of various neurotransmitters of the progress of many diseases where the function of the central nervous system would be the most altered. The involvement of dopamine in various aspects of function of the CNS has been widely recognised for a relatively long period of time and there were many hypotheses suggested regarding its role in the disorders that involve the inclusion of mechanisms of reinforcement, cognition alterations, psychological alteration and other types of disturbances of the neurological system. As this particular neurotransmitter can be found functioning in many areas of the brain, its wold be hard to embrace all the aspects of manipulations with dopaminergic system and its pathways, therefore, in this work we will mostly focus on the role of presynaptic modulations of the dopaminergic pathways in such disorders as psychosis and addiction in humans. The studies that are going to be reviewed show reliable explanations of the origins of dopaminergic hypotheses for the discussed disorders, while the review of the possible treatments that involve targeting the presynaptic part of the dopaminergic pathways would also support the hypothesis and bring us to the conclusion of the usefulness of these therapeutic manipulations.

Keywords: Dopamine; Presynaptic modulation; Psychosis; Addiction; Neurotransmitter

Evaluation The Effect of Several Factors on The Extraction Yield of Mycosporine-Like Amino Acids from Fischerella Sp.

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21-23 February 2023

Poster: P107

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Abstract

The bioactive metabolites produced by microalgae and cyanobacteria are excellent sources for the biomedical industry. One of the ultraviolet-absorbing metabolites, known as mycosporine-like amino acids (MAAs), have a structure similar to amino acids. MAAs have been demonstrated for other activities, such as antioxidant and anti-inflammatory effect. Extraction of MAAs from natural sources such as cyanobacteria have been an attractive field of research. We previously introduced two species of *Fischerella* sp. as the source for production of MAAs. Several effective factors might influence the extraction process and purification yield of MAAs, including time, temperature, sonication and type and volume of solvent. This study used experimental design to optimize MAAs extraction from *Fischerella* sp. The best level of five parameters, including total extraction time, temperature, sonication duration, methanol concentration, and solvent volume, were predicted using central composite design. Using the DPPH radical scavenging assay, the antioxidant effect of the extract was evaluated. Results: The main compounds detected in extraction product showed a maximum absorbance around 335 nm, with a mass to charge ratio of about 344 m/z, which is highly similar with the characteristics of Mycosporine-glycine-valine. However, many of samples showed more than one peak with maximum absorbance at 300-400 nm. Several other compounds have been detected in HPLC chromatogram with no maximum absorption at this range. Maximum MAAs% extracted from *Fischerella* sp. reached to 89% of total extraction compounds in final extracts, and antioxidant activity were calculated to reach the maximum level of 59.3%. Nevertheless, there was no significant model to associate extraction condition with MAA% in final extract or antioxidant activity of final extract. However, using area under curve of peaks with maximum absorption at 300- 400 nm, as an index for MAAs amount, resulted to a significant model in which all of the parameters had a positive impact on the MAA extraction. Several other factors may have affected the MAAs extraction efficiency and MAAs' related bioactivity, adding other chemicals or surfactants. In order to produce an extract with desired bioactivity, more research will be done in future studies to identify the precise elements influencing the MAAs' extraction.

Keywords: *Fischerella* sp; Mycosporine-like amino acids; Extraction; Experimental Design; Optimization

Cloning and Expression of Thioredoxin-Myelin Oligodendrocyte Glycoprotein Fusion Protein in A Prokaryotic Host

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21-23 February 2023

Poster: P108

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Abstract:

Myelin oligodendrocyte glycoprotein (MOG) is an inducer of experimental autoimmune encephalomyelitis (EAE) in animals. EAE is the most commonly used animal model in MS research and development of a number of its treatments. Here, TRX tag - MOG fusion protein was expressed in E. coli BL21 (DE3). A codon optimized gene expressing MOG was cloned in pET32a(+). The construct was transformed and expressed in the E. coli. Transformants were grown in LB Broth medium at 37°C. Protein expression was induced by addition of 1 mM IPTG at OD600 = 0.7. Constructed plasmid was approved by polymerase chain reaction (PCR) and restriction enzyme analysis. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and western blot analysis using mouse anti-6XHis tag antibody showed an estimated 32.5 kDa-size protein band corresponding to the recombinant MOG-Thioredoxin fusion protein. These findings imply the ability of E.coli in the expression of recombinant MOG-Thioredoxin fusion protein which may be used in EAE model induction.

Keywords: MOG; E.coli; expression; multiple sclerosis

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Dendritic Cell Vaccines for Colorectal Cancer: A Systematic Review

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21-23 February 2023

Poster: P109

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Abstract:

A number of recent studies have focused on dendritic cells, which present antigens and integrate adaptive and innate immunity to initiate antitumor immunity. In terms of immunotherapy, DCs (dendritic cells) have tremendous potential. Dendritic cells have been shown to be effective in producing host immune responses against tumor antigens in cancer vaccines for CRC (colorectal cancer) patients. FDA recently approved the first DC-based cancer vaccine for hormone-refractory prostate cancer (Sipuleucel-T, Provenge), which has revived hopes about DC-based cancer vaccines in the future. However, more research on DC biology and host-tumor interactions is needed to translate this knowledge into more selective and clinically effective DC-based immunotherapy strategies for cancer. During the past 20 years, DC-based immunotherapy has been the focus of considerable Phase I and II clinical researches, resulting in evidence that shows DC-based immunotherapy is a promising approach for cancer treatment. The DC-based vaccine has been used in an increasing number of patients, but only a small fraction of patients showed immune responses and few (10%–15%) showed clinical benefit. As well, only a few cases have reported a correlation between the immune and clinical responses, leaving the question open as to whether the observed responses are a consequence of vaccination or just better conditions that prime the immune system. A large amount of data was left inconclusive due to the heterogeneity of DC preparation and vaccination protocols, as well as the use of various antigens and loading techniques. Recent clinical trials have led to several important insights that may aid in developing more effective DC-based vaccines. A search on PubMed and web of science databases was performed. The strategy for literature search was represented by “((cancer vaccine and colorectal cancer) or (dendritic cell vaccine and colorectal cancer))” on Pubmed.gov and “dendritic cell vaccine and colorectal cancer” on web of science. The studies selected from both databases were original articles and systematic reviews. Duplicated papers were excluded. Further analysis of the abstracts and full texts was conducted. The articles which did not focus on our topic were removed. Results: our search found 19 articles in PubMed and 26 articles in web of science. A total of 40 articles were excluded because they did not meet our inclusion criteria. On the whole, 5 articles were included. Dendritic cell (DC) vaccines are used to treat advanced colorectal cancer (CRC). Due to DC incompetence, vaccine-induced clinical responses have not always been satisfactory. A variety of complex issues should be discussed for this therapy to achieve its full potential such as DC generation and maturation, antigen sources, DC loading methods, and DC administration methods.

Keywords: colorectal cancer; dendritic cell vaccine; immunotherapy; cancer vaccines

FTIR Spectroscopy Application Evaluation for The Diagnosis of Cancer in Human Stomach Tissue

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21-23 February 2023

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Stomach cancer has been identified as the fifth most deadly cancer in humans. Among its diagnostic methods, including biopsy through endoscopy and radiography with contrast. Patients with stomach cancer generally do not have specific symptoms, and for this reason, their disease is diagnosed late. On the other hand, FTIR spectroscopy gives us the task of examining biological changes at the biomolecular level. For this reason, we sought to distinguish cancerous tissues from healthy tissues using this method. After collecting 30 fresh stomach tissue samples, the tissues were transferred to the cell culture laboratory as soon as possible without adding substances such as Normal saline or Formalin, and the spectrum of the fresh tissue was analyzed by an FTIR- ATR device with a resolution of 2 cm^{-1} and 100 times of scanning. Then the spectra were statistically analyzed. After processing the spectras, 185 peaks with $r=0.98$ were observed in healthy sample tissues, 171 peaks with $r=0.98$ in cancer sample tissues, 177 peaks in cancerous and healthy samples and 226 peaks with $r=0.97$ in inflammatory samples. In the average spectra, 43 peaks were specifically related to cancerous tissues and 34 peaks were specifically related to healthy tissues. Considering the acceptable shift up to 3 cm^{-1} , five peaks had a shift of $\pm 3\text{ cm}^{-1}$, twenty peaks had a shift of $\pm 2\text{ cm}^{-1}$, and twenty peaks had a shift of $\pm 1\text{ cm}^{-1}$. According to the resolution of 2 cm^{-1} , the ± 3 and $\pm 2\text{ cm}^{-1}$ shifts are more valuable. Regarding the absorption height, there were 20 common peaks in healthy and cancerous tissues, of which 6 peaks had significant differences. According to the comparisons, the highest level of differentiation between healthy and cancerous tissues is in the range of $1666\text{--}1691\text{ cm}^{-1}$ with 100% difference in the absorption area of proteins related to the amide I region and then in the range of $2766\text{--}2777\text{ cm}^{-1}$ with 66.66% difference. It was observed in the absorption area of lipids. Finally, it can be said that by using this method, cancerous tissues can be distinguished from healthy tissues.

Keywords: FTIR Spectroscopy; ATR; Gastric Cancer; Stomach; Inflammation

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Novel Approaches of Network Pharmacology in The Drug Response and Treatment of Lung Cancer: A Systematic Review

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21-23 February 2023

Poster: P111

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Abstract:

The term " network pharmacology" can be considered as s pioneering drug repurposing technique in complex systems. In other words, the application of network pharmacology is summarized by associating big data and analyzing it to interpret biological systems. However, some studies highlighted it with different concepts, such as Systematic Pharmacology or Drug-Target Networks. Primarily, studies on these topics have heterogeneity in information, and various diseases were covered. Therefore, this review tries to bring data from scattered recent research studies to treat specific cancers, such as lung cancer. Methods: This study was conducted according to the section on systematic reviews. Web of Science, Scopus and Pubmed were scanned. After excluding review articles, book chapters and conference papers based on inclusion and exclusion criteria, only seven eligible articles remained for data synthesis. Finally, studies were analyzed and reviewed on the cornerstone of the PRISMA method. Results: Comparisons among seven studies revealed that the utilization of different databases like STITCH, TCMSP, and BATMAN-TCM could be beneficial in finding a related the target for cancer treatment. The selected studies demonstrate that cinobufotalin, ginseng and Qingfei Jiedu decoction have significant effects on lung cancer by regulating the expression of some genes, such as VEGFA, EGFR, CASP3, and AKT1. Consequently, a few results used further information from gene-linked pathways like apoptosis and screening materials to earn better network pharmacology models. Conclusion: According to more and more growth of novel systems to real-world challenges in the field of cancer pharmacology, it is expected to see the promising implementation of system pharmacology into precision medicine, which can go Beyond personalized medicine. Also, it may increase the chance of cure in patients with cancer.

Keywords: network pharmacology; Drug-target network; lung cancer

Protective Effect of Dapsone Against Bleomycin-Induced Lung Fibrosis in Rat

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21-23 February 2023

Poster: P112

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Abstract:

Idiopathic pulmonary fibrosis (IPF) is a long-term interstitial lung disease that manifests as symptoms like asthma and coughing. Oxidative stress and inflammatory factors are the culprits. A chemotherapeutic drug called bleomycin (BLM) induces an *in vivo* model of IPF. Due of dapsone's effects on inflammation and oxidative stress in adult male Wistar rats, we looked at how it affected IPF that had been brought on by bleomycin. Five groups (Control, BLM, BLM + dapsone 1, BLM + dapsone 3, and BLM + dapsone 10) of animals were created at random. Normal water and food were given to the control group. Bleomycin (BLM) (5 mg/kg) was administered intratracheally to the fibrosis group in order to induce pulmonary fibrosis. One hour after receiving BLM, three groups of rats were given daily treatments of 1, 3, and 10 mg of dapsone intraperitoneally for two weeks. To assess bleomycin and the therapeutic effect of dapsone, the activities of the antioxidant enzymes superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), as well as oxidative stress markers myeloperoxidase (MPO), malondialdehyde (MDA), protein carbonyl (PC), and nitrite, were measured. Hematoxylin-eosin (H & E) and Massons trichrome staining were used for the lung tissues histological analyses. BLM decreased oxidative enzyme activity and raised oxidative stress indicators, but dapsone therapy reversed the effects. The overall amount of inflammatory cells, including neutrophils and eosinophils, was also looked at. These cells appeared to be enhanced by BLM and diminished by dapsone. Dapsone reduced lung fibrosis brought on by BLM, alveolar wall thickness, and inflammation, according to the results of H&E and Massons trichrome staining. Dapsone appears to treat pulmonary fibrosis, according to the study's findings, by reducing the toxic effects of bleomycin and having anti-inflammatory and anti-oxidative stress properties.

Keywords: Pulmonary fibrosis; Bleomycin; Dapsone; Oxidative Stress; rat.

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In Vitro Evaluation of Cytotoxic Effects of Mutated Form of Soluble IL-6R in Ovarian Cancer Cell Line

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21-23 February 2023

Poster: P113

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Abstract:

Ovarian cancer is the fifth leading cause of cancer deaths among women (1). Inflammatory mediators, especially IL-6, play an important role in cancer metastasis (2). Therefore, it seems that interleukin-6 inhibition can act as an anticancer agent. In our previous study, the soluble form of the IL-6 receptor containing targeted mutations (mIL-6R) was produced with recombinant DNA technology and it was proved by the ELISA test that its affinity for interleukin-6 is higher than the natural form of the receptor. Also, its tendency to form a heterodimer with the second part of the receptor, which is called gp130 and is involved in signal transduction, decreased significantly (3). In this study, the cytotoxic and inhibitory effects of mIL-6R were investigated at the molecular level on ovarian cancer cells after determining the best condition for its soluble expression as well as purification. Materials and methods: Production of mutant IL-6 receptor (mIL-6R) in E.coli BL21 fused with intein 1 of ptwin-1 vector using IPTG inducer and optimization of expression conditions based on inducer concentration, induction temperature and duration of incubation was performed. Purification of the expressed protein using the IMPACT system and optimization of the purification process in terms of incubation temperature, cleavage buffer pH and incubation time was also surveyed. In each step, SDS-PAGE method was used to evaluate the recombinant protein band. Finally, determining the cytotoxic effects of mIL-6R protein on OVCAR-3 cancer cell line was investigated for 72 hours toward Tocilizumab as the positive control using MTT assay method. Results: The highest amount of soluble protein was obtained at 20°C with a concentration of 0.5 mM IPTG. The highest amount of protein purification was observed at 25°C, 24 hours of incubation and at pH = 4. mIL-6R protein had a cytotoxic effect on the OVCAR-3 cell line with IC₅₀ value as about 36.8 mcg/ml. Conclusions: Recombinant mIL-6R protein by binding to IL-6 and preventing the binding of this cytokine to its receptor on the cell surface has a similar effect as Tocilizumab (an IL-6 inhibitory antibody) and has been effective in reducing the inflammatory process of ovarian cancer. This protein has been as effective as Tocilizumab in this cell line. according to the inhibitory effects of this protein on the signal transduction pathway caused by interleukin-6, relevant preclinical tests can be started to use this protein as an anticancer drug candidate.

Keywords: interleukin-6; IL-6; OVCAR-3; ovarian cancer; IL-6 mutation protein.

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Phytochemical, Antioxidant, and Antimicrobial Studies on *Quercus Castanifolia*

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21-23 February 2023

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Abstract:

Quercus spp. a noteworthy genus of the beech family, Fagaceae, with over 450 species is widely distributed in Asia, Europe, America, and North Africa (1). *Quercus* constitute more than half of Irans forests, which are geographically located in the northern areas of Alborz and the Zagros Mountain range in the west, including *Quercus robur*, *Q. petraea*, *Q. infectoria*, *Q. cedrorum*, *Q. komarovii*, *Q. longipes*, *Q. macranthera*, *Q. brantii*, *Q. castanifolia* (2). *Quercus* fruits, generally known as acorns, have been used for animal feeding and human diet due to their high nutritional values (3). Additionally, since of the presence of biologically active ingredients, it is also employed in traditional medicine. So far, various compounds such as alpha-tocopherol and other fatty acids, tannins, flavonoids, and phenolic acids (e.g., tannic acid, gallic acid, ellagic acid, and caffeic acid) have been isolated from several acorn species. Moreover, studies have shown a wide range of activities such as antimicrobial, antioxidant, anti-inflammatory, antidiabetic, antibiofilm, and anticancer activities for acorns (4). Acorns were collected in November 2021 in Sari, Iran (northern of the country), identified, and deposited as *Quercus castanifolia* in a local herbarium. It was then dried, peeled, powdered, and extracted by maceration using aqueous methanol (70%, v/v). Afterward, a variety of analyses were conducted on the obtained extract, including starch, protein, fatty acid, and tannin contents. Total phenolics content was also determined by Folin-Ciocalteu while antioxidant and antibacterial activity was tested using DPPH free radicals scavenging and agar diffusion assay. Results: Acorns experimentally presented a high amount of starch, but protein and fat contents were low. Its most fatty acids were found as oleic acid and linoleic acid. The total phenolic content of acorn extract was 180 mg/g of the dried weight on the basis of gallic acid. Moreover, the amount of tannin, an important type of polyphenol, was about 7%. Likewise, it exhibited an impressive antioxidant activity of 87%. The extract displayed detectable antibacterial activity against *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Staphylococcus epidermidis*. The *Q. castanifolia* acorn extract is a great source of phytoconstituents, especially polyphenols which can be exploited for their antioxidants and antimicrobial potential activities and can be used in diverse research fields, such as pharmaceutical, nutraceutical, and medical sciences. Large areas of oak forests, high availability, and their drought resistance make *Quercus* species important available sources of bioactive compounds.

Keywords: Acorn; *Quercus castanifolia*; phytochemical composition; Antioxidant; Antimicrobial effect.

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The Therapeutic Effect of Methanolic Extract *Bryonia dioica* Jacq. in a Female Rat Model of Polycystic Ovary Syndrome

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21-23 February 2023

Poster: P115

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Abstract:

Polycystic ovary syndrome (PCOS) is one of the most common endocrine diseases that affects 5%–10% of women of childbearing age. Several factors contribute to the development of PCOS such as dysfunction of the hypothalamic–pituitary axis and ovarian function, as well as increased insulin levels. The manifestations of the disorder include a wide range of symptoms, including menstrual disorders, acne, infertility, and increased body fat. Currently, the most well-known treatments for PCOS are clomiphene, metformin, letrozole, and tamoxifen. Due to their side effects, the identification of substitute drugs is essential. One of the traditional medicines, which is usually used in different parts of the world, particularly in Western Europe, is *Bryonia dioica* Jacq. (*B. dioica*). This plant is used in the treatment of disease due to its active ingredients like polyphenols. **Materials and Methods:** Induction PCOS in a female rat (3 weeks old) was performed through subcutaneous injection of testosterone enanthate (1 mg/100g) daily for 35 days. The effects of *B. dioica* (30 and 60 mg/kg) root methanolic extract on PCOS-induced rats were evaluated after 28-day treatment. On the last day, the serum levels of follicle-stimulating hormone (FSH), glucose, low-density lipoprotein/high-density lipoprotein (LDL/HDL), luteinizing hormone (LH), and testosterone and histological studies (hematoxylin and eosin [H&E] staining) were measured. Results showed that FSH and LH levels ($P < 0.05$) as well as glucose ($P < 0.001$) in the *B. dioica* groups normalized significantly compared to the PCOS group. LDL levels decreased in rats and the LDL/HDL ratio decreased in all treatment groups. In histologic assay, metformin and *B. dioica* restricted the effects of testosterone in the ovaries of rats. The data indicate that methanolic extract of *B. dioica* recovers hormonal factors in PCOS.

Keywords: polycystic ovary syndrome; methanolic extract; *Bryonia dioica* Jacq

Omidubicel: A New Approach Based on Cell Therapy for The Treatment of Hematologic Malignancies

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Poster: P116

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Abstract:

Abstract Umbilical cord blood (UCB) is recognized as an essential source of hematopoietic stem cells (HSCs) for use in allogeneic HSC transplantation in blood-related malignancies. However, cord blood transplantation is associated with challenges, including delayed hematopoietic recovery, prolonged hospitalization, and higher transplant costs than other donor sources. Recently, a new treatment method has been proposed to solve this problem. Omidubicel is an advanced nicotinamide-based cell therapy made from a single HLA-matched cord blood unit for each patient. This method is associated with rapid transplantation in patients with blood malignancies. In this method, cells are obtained after ex-vivo selection of CD133+ cells from a cord blood unit for 21 days in the presence of small molecules of nicotinamide and other growth factors. According to a recent phase III clinical trial report (NCT02730299), patients who received omidubicel had a faster time to neutrophil engraftment and platelet recovery, fewer infections, and shorter hospital stays than patients who received standard cord blood transplants. Omidubicel reduces neutrophil recovery time by ten days and average platelet recovery time by 13 days. It also effectively reduces the incidence of infectious complications and the number of days spent in the hospital after transplantation. The reduced risk of viral infections for omidubicel recipients was an unexpected finding and may be attributed to more vital NK cell regeneration. This review article discusses the details of this new method based on cell therapy.

Keywords: Omidubicel; Umbilical Cord Blood; Nicotinamide; CD34+, CD133+.

Luteolin Inhibits Breast Cancer Cells' by Androgen and Beta Estrogen Receptors; An In-Silico Study

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Poster: P117

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Abstract:

According to a report by the National Cancer Institute, breast cancer (BC) was the most prevalent new cancer incidence in 2022 and the most common cancer in women, with a mortality rate of 15%. The use of herbs and phytochemicals is one of the first methods employed by humans to deal with ailments. Flavonoids are a class of naturally occurring plant substances that significantly affect cancer cells by increasing apoptosis and cell toxicity. Luteolin, also known as 3,4,5,7-tetrahydroxy flavone, is a flavonoid in various food plants, including broccoli, onion, celery, carrot, parsley, etc. This study used Pubchem, Binding DB, GeneCards, Way2Drug, DAVID, and DisGeNET to identify BC-related luteolin targets. The String database enabled us to explore protein-protein interactions of BC-related proteins under the influence of luteolin and the gene ontology of these proteins. Cytoscape 3.7.2 illustrated the data network. The gene ontology data revealed that protein binding, plasma membrane, and response to xenobiotic stimulus are the most probable processes under the influence of luteolin. According to network pharmacology, AR (Androgen receptor) and ESR2 (beta Estrogen receptor) are the most influential targets in relation to BC. Due to the KEGG pathway, this compound has the most significant effect on BC among Cancers. In addition, estimations demonstrated that they are more effective against the MCF7 cell line. Recent research has demonstrated that luteolin can reduce the growth of BC cell lines by inhibiting AR and the increasing expression of ESR2 and ESR1. Moreover, additional studies validate our finding on luteolin activities as a metastasis suppressor and apoptosis inducer in BC cell lines. Considering the results and the most recent study, luteolin appears to be a potent agent against several breast cancer cell lines with multiple pathways that produce tumor and metastasis suppression.

Keywords: Network Pharmacology; Breast Cancer; Luteolin; Androgen Receptor, Estrogen Receptor

Reference:

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Study Effect of Mono Sodium Glutamate Exposure During Pregnancy on Causing Autism in Male Offspring Rats

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Poster: P118

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Abstract:

Autism spectrum disorder is associated with a combination of genetic and environmental factors. Today, researchers exploring the chemicals found in consumer products that are suspected to contribute to autism. It has been proven that monosodium glutamate had toxic effects. Considering the pathways of autism pathogenesis and its overlap with the neurotoxicity pathways caused by monosodium glutamate, investigating the relationship between the pregnancy exposure to this compound and the autism development in the children seems necessary. Therefore, aim of this study is to investigate the effect of monosodium glutamate during pregnancy on the autism development in male rat offsprings. Methods: Pregnant rats were divided randomly into five groups. The first group was the control group in which animals received oral normal saline. Group 2, 3 and 4: Pregnant rats received different doses (1.5, 5, and 10 g/kg) of monosodium glutamate orally respectively. Group 5 received Valproic acid (VPA) for inducing autism model. The monosodium glutamate administered through oral gavage on a daily basis from day 1 to day 18 of pregnancy. After childbirth and weaning after 21 days, different behavioral tests including marble burying, self- grooming, and Barnes maze test were used to evaluate anxiety, repetitive movements, and spatial memory function in offsprings. Results: The results showed that monosodium glutamate similar to VPA led to the induction of autistic anxiety and repetitive behaviors. It could also deteriorate the spatial memory in rats. Another finding was the dose-dependent manner of monosodium glutamate in inducing autism, so that behavioral symptoms potentiated with increasing monosodium glutamate dosage. Findings of present study indicated that monosodium glutamate was able to significantly induce autism in rats in a dose-dependent manner. Consequently, monosodium glutamate might be a harmful compound that should be avoided during pregnancy.

Keywords: Pregnancy; Monosodium glutamate; Autism.

Reference:

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Evaluation of Cytotoxic Effect of Total Extract of *Daphne Mucronata* in Breast Cancer Cell Lines

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21-23 February 2023

Poster: P119

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Abstract:

Daphne mucronata is a wild shrub that belongs to the family Thymelaeaceae. It is considered as an important medicinal plant because of its ethnomedicinal and pharmacological uses. *D. mucronata* is used in folk medicine to treat skin disorders, ulcers, and bone diseases. Besides, this plant has shown antimicrobial activity and antioxidant properties. (1) Materials and methods: In the present study, we have tested the total extract (methanol: water: 80:20) of *D. mucronata* leaves in two breast cancer cell lines (MCF-7 and T-47D) using the MTT assay. The MTT assay involves the conversion of the water-soluble yellow dye MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] to an insoluble purple formazan by the action of mitochondrial reductase. (2) Results: The extract has shown cytotoxic activity against breast cancer cell lines MCF-7 (IC₅₀=201.552 µg/mL), and T-47D (IC₅₀=245.856 µg/mL). While Etoposide as Positive control has demonstrated cytotoxic activity against breast cancer cell lines MCF-7 (IC₅₀=28.18µg/mL) and T-47D (IC₅₀=27.92µg/mL). The comparison of results has revealed that cytotoxicity exhibited by 80% methanol extract of *Daphne mucronata* might have low activity. Conclusions: The total extract of *D. mucronata* is moderately cytotoxic toward MCF-7 and T-47D cells. According to the results of this study, it is suggested that more experiments be performed to more accurately investigate the cytotoxic effects of different fractions and active substances in *D. mucronata*.

Keywords: *Daphne mucronata*; cytotoxic; MTT assay; total extract.

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***Salvia hypoleuca* Essential Oil Effects on Breast Cancer: A Network Pharmacology Perusal.**

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21-23 February 2023

Poster: P120

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Abstract:

Breast cancer was the most frequently diagnosed type of cancer in Iranian women, based on a National Cancer Institute 2022 report. It is considering the various costs that cancer imposes on society and the costs that it enforces on individuals financially. With this mentality, the importance of new herbal treatment methods that can be established based on the findings of one nation's ancestors in traditional medicine documentation is much more remarkable.

Salvia hypoleuca is an annual flowering herb from the Lamiaceae family, endemic to Tehran and Mazandaran provinces, Iran. It has been utilized in Persian traditional medicine (PTM) as an anti-inflammatory, antispasmodic agent. Due to the inflammation role in the cancer process, it could be a candidate to find new potencies effectual in cancer inhibition.

We scrutiny the Google Scholar to find this plants EO Compounds. Pubchem, Binding DB, GeneCards, Way2Drug, and DisGeNET were put to use to identify the probable breast cancer-affecting targets of *S. hypoleuca* EO. Cytoscape 3.9.1 developed the data network.

The scrutiny demonstrated 78 compounds in *S. hypoleuca* EO. The Gene Ontology results that positive regulation of transcription from RNA polymerase II promoter, nucleoplasm, and enzyme binding are the most probable effects of *S. hypoleuca* EO. Among the chemicals identified in EO, cis-Cadin-4-en-7-ol and α -Cadinol are the most influential compounds. Estrogen receptor β (ESR2) and androgen receptor (AR) are the most effectual targets based on network pharmacology.

ESR2 has an undeniable effect on breast cancer by affecting Oestrogen signaling and induction of 17 β -oestradiol, which enhances aromatase activity. AR expression stimulates proliferation in triple-negative breast cancer, whereas; its performance depends on the tumor microenvironment.

According to the results and usage of the *Salvia* genus in PTM to relieve menopausal symptoms, *S. hypoleuca* could be a potent agent against sex hormone-related cancers, especially breast cancer.

Keywords: Breast Cancer; *Salvia hypoleuca*; Network Pharmacology; Estrogen Receptor Beta; Androgen Receptor

Reference:

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Quantification of Total Phenolic Content, Total Flavonoid Content, and Anticonvulsant Activity of Common Hop Crude Extract and Different Fractions

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21-23 February 2023

Poster: P121

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Abstract:

Epilepsy is a condition that affects the central nervous system and causes frequent seizures. It is estimated that more than 50 million individuals around the world are affected by epilepsy (1). In addition, 20–30% of patients are resistant to the common treatments of epilepsy. Although various medicines from different categories are utilized to control epilepsy, these medicines are always associated with many side effects (2). Therefore, it seems necessary to discover new natural compounds to reduce the complications or side effects of antiepileptic drugs. Given this and the traditional use of common hop (*Humulus lupulus* L.) for the treatment of different neurological disorders, this study was carried out to determine total phenolic content (TPC) and total flavonoid content (TFC) as well as antiseizure activity of crude extract and different fractions of *Humulus lupulus* L. aerial parts. Materials and methods: In the current study, the dried and powdered aerial parts of *Humulus lupulus* L. were extracted by the maceration method using ethanol 96%. The obtained crude extract was then extracted with different solvents of increasing polarity, starting from n-hexane followed by ethyl acetate, ethanol, and water through ultrasonic-assisted extraction. The obtained extracts were then tested for antiseizure activity using PTZ (pentylenetetrazole) test (3). Besides, the total phenolic and total flavonoid contents of the mentioned extracts were determined using Folin-Ciocalteu and aluminum chloride reagents, respectively. Results: In the PTZ test, the ethanol fraction at 400 mg/kg and 800 mg/kg showed 60% and 80% protection against PTZ-induced seizure which was statistically significant compared to the control group (p-value

Keywords: Anticonvulsant; Extract; Hop; Mice; Seizure.

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Potentials of Aquaponics System for the Development and Production of Medicinal Herbs

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21-23 February 2023

Poster: P122

Abstract Presenter:

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Abstract:

Aquaponics systems integrate fish production and hydroponic plant production simultaneously, where fish waste is used as nutrients for various vegetable crops. Many herbaceous plants such as basil, peppermint, Jute, Chamomile, Parsley, and spearmint have been reported to grow in aquaponics systems. However, very few research findings are available on the environmental requirements of these herbs in aquaponics systems in relation to active ingredients and other metabolites. This is because aquaponics is usually placed under shade, and LED light bulbs could be used to supply additional light to the system. In addition, some aromatic herbs may develop varied levels of aromaticity considering the nature of the aquaponics environment. Apart from light, aquaponics also grows plants in a soilless environment. Herbs whose root parts are exploited for therapy may differ in metabolite activities compared with soil-grown specimens. While the growing of medicinal plants in aquaponics may afford easy access to home remedies and safety from a confusing array of herbal medicine in the market. Research is needed on the quality of herbal plants from aquaponics sources.

Keywords: Aquaponics; medicinal plant; production.

Microscopic Examination of the Nodes and Internodes of Lablab Purpureus L. Sweet.

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Poster: P123

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Abstract:

Lablab purpureus L. Sweet., (Fabaceae), grown in the conditions of central Russia as an annual ornamental plant, has prospects for use as a medicinal plant material. The study of the anatomical and diagnostic features of Lablab purpureus L. Sweet., especially the nodal anatomy, is of taxonomic importance. The distinguishing features of the node include: the number of bundles of the leaf trace, the features of the formation of the gap and the sequence of introduction of the leaf and branch traces into the stem. The purpose of this study is to identify the diagnostic features of the structure of the node and internodes of the stem of Lablab purpureus L. Sweet. For this, microscopy of Lablab purpureus L. Sweet. stems fixed in 70% ethanol solution were carried out basipetally from one internode to another. As a result, it was revealed that on the transverse section, the stem of Lablab purpureus L. Sweet., round in shape, is covered with epidermis. The primary cortex is differentiated. The central axial cylinder begins with a pericyclic sclerenchyma, located in areas above open collateral vascular bundles, in the phloem of which there are essential oil receptacles. The xylem lies in a continuous layer due to the presence of a libriform between the bundles. Transitional stem. There are 5 vascular bundles in the petioles of the leaf, all of them enter the vascular system of the stem, but in a different order: first, the synthetic bundle, formed by the median bundle of the leaf and bundles of the branch trace, enters, and then the lateral bundles of the leaf form their own gaps. Thus, the node is five-lacun, five-beam. The data obtained can be used in the taxonomy and phylogeny of the Fabaceae family, as well as for the identification of promising medicinal plant material Lablab purpureus L. Sweet.

Keywords: Lablab purpureus L. Sweet.; Nodal anatomy; Node; Internode; Synthetic bundle; transitional stem type.

Reference:

1. Yusuf S.M., Fedorova L.V. The Nodal anatomy of leaf of Lablab purpureus L. Sweet. Prospects for the introduction of innovative technologies in medicine and pharmacy: collection of materials of the IX All-Russian scientific and practical conference with international participation, November 25, 2022 - Elektrogorsk: "ECOLab"; Orekhovo-Zuevo: GGTU, 2022. 281-286.

Research of Antioxidant Properties of Intravaginal Remedy with Humulus Lupulus Extract

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21-23 February 2023

Poster: P124

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Abstract:

Intravaginal biodegradable collagen plates (BCP), which have positive properties: simplicity of composition and technology, stability during storage, a combination of adhesion and moisture absorption, uniform distribution in the vaginal fluid, excretion naturally without additional rinsing and douching, are promising for the prevention and treatment of gynecological diseases. BCPs have osmotic activity and have biopharmaceutical advantages, in particular, high bioavailability associated with significant bioadhesion, which makes it possible to prolong the action of biologically active substances (BAS). The source of the BCP was Humulus Lupulus (HL). Complex pharmacological effects (anti-inflammatory, antioxidant, antimicrobial, capillaroprotective, phytoestrogenic, analgesic) are caused by a complex of biologically active substances (BAS): polyphenolic compounds (flavonoids, catechins, phenol carboxylic acids, oxycoric acids, phytoestrogens), bitter glycosides (derivatives of acylfloroglucides (AFG) – humulone, lupulone, etc.), essential oils and terpenoids. The purpose of the research was to evaluate the antioxidant activity of BCP with Humulus lupulus extract (HLE).

Keywords: Humulus lupulus; Antioxidant properties; Antioxidant.

Improving Quality Indicators of the Bidens Tripartita Herb

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21-23 February 2023

Poster: P125

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Abstract:

Purpose: to study the quantitative content of biologically active compounds of the B. tripartita herb. To assess the content of polysaccharides (gravimetry) and flavonoids (SP), the methods described in the SP RF XIV edition for the B. tripartita herb were used. A modified PSC method (SP) was also used. The total flavonoids content was 0.7-1.2%, PSC - 4.1-7.5% (gravimetry), 3.8-7.2% (SP). The results of determining PSC by the pharmacopoeial and modified methods are comparable. Rutin (absorption maximum at 415 nm) was confirmed as a standard (according to experimental UV spectra).

Keywords: Bidens tripartita L.; Polysaccharides; Flavonoids; Rutin; Gravimetry; Spectrophotometry.

Reference: <https://doi.org/10.29296/25419218-2022-02-04>.

Honeysuckle Edible (*Lonicera Edulis* Turcz. Ex Freyn) as a Rich Source of Polyphenolic Compounds

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21-23 February 2023

Poster: P126

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Abstract:

Honeysuckle edible (*Lonicera edulis* Turcz. ex Freyn) as a rich source of polyphenolic compounds Gerasimov M.A., Rodionova G.M The fruits of honeysuckle (*Lonicera edulis* Turcz. Ex Freyn) are currently being widely studied in many countries around the world. Researchers are particularly interested in honeysuckle fruits, which is due to such factors as taste, early ripening, high content of biologically active substances (BAS) of a polyphenolic nature, such as anthocyanins and proanthocyanidins. [1, 2]. Anthocyanins and proanthocyanidins have a number of beneficial properties. They are antioxidants, have anti-inflammatory, antimicrobial, hypolipidemic and hypoglycemic properties [1, 2]. Thanks to these properties, honeysuckle fruits are a suitable raw material for both the pharmaceutical and food industries. Materials and methods. The objects of the study were frozen honeysuckle fruits of 10 varieties: "Bakcharsky Giant", "Morena", "Aurora", "Blue Cliff", "Nymph", "Blue Banana", "Borealis Blizzard", "Borealis Beauty", "Indigo Jam", "Commonwealth" originating from Russia, Canada and America. Honeysuckle was grown on the basis of the Federal State Budgetary Scientific Institution "FNTs im. I.V. Michurin. The fruits were thawed, ground in a household blender to a mushy state, then extraction was carried out. Anthocyanins were extracted from raw materials with 70% ethanol acidified with 0.1 M hydrochloric acid solution in an ultrasonic bath at room temperature. Extraction of proanthocyanidins was carried out with 60% methanol in a boiling water bath under reverse refrigerator. The determination of the content of monomeric anthocyanins in terms of cyanidin-3-glucoside was carried out by pH-differential spectrophotometry, the content of proanthocyanidins in terms of procyanidin B2 was determined by the modified Bate-Smith method. Anthocyanin profiles were determined by HPLC with diode array spectrophotometric and mass spectrometric detection. Results and discussion. Significant differences in the content of biologically active substances were observed between the studied varieties. Anthocyanins: The total content of anthocyanins ranged from 198.3 mg/100 g (hereinafter: wet weight) in Aurora to 567.9 mg/100 g in Indigo Jam, the average content was 383.1 mg/100 g. The profile of anthocyanins is represented by glycosides of cyanidin, peonidin and pelargonidin with a significant predominance of cyanidin-3-glucoside (82.1%-89.2% of the total anthocyanins). Proanthocyanidins: Significant amounts of proanthocyanidins were found in the studied varieties of honeysuckle, ranging from 478.2 mg/100 g in "Bakcharsky Giant" to 1590.9 mg/100 g in "Nymph" with an average content of 1034.5 mg/100 g. Conclusion. A systematic study of the content of anthocyanins and proanthocyanidins in honeysuckle fruits was carried out. Since the berries were grown under the same conditions, it can be concluded that the amount of accumulated biologically active substances directly depends on the variety of honeysuckle. According to the results of the study, promising varieties "Indigo Jam", "Nymph" were selected, which are distinguished by a high content of these BAS groups.

Keywords: *Lonicera Edulis*; Anthocyanins; Proanthocyanidins.

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Determination of Numerical Indicators of Oil Extract of Artemisia Cina

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21-23 February 2023

Poster: P127

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Abstract:

Artemisia cina is an endemic plant that grows in the Turkestan region in the valleys of the Syrdarya and Arys rivers. The department of pharmaceutical and toxicological chemistry of the South Kazakhstan medical academy has developed a method for obtaining oil extract of *Artemisia cina*. An important aspect of the creation and introduction of oil extracts into medical practice is the determination of numerical indicators that guarantee the quality of the drug and its compliance with the requirements of regulatory documents. The determination of numerical indicators was carried out in accordance with the requirements of the State Pharmacopoeia of the Republic of Kazakhstan (SP RK). The study of the main quality indicators and standardization of the oil extract were carried out on laboratory samples of phytopreparation. The oil extract is a transparent oily liquid of light green color with a specific odor characteristic of the raw materials used according to 5 series of laboratory samples. To control the oxidation processes of the oil extract, the SP RK regulates the determination of such numerical indicators as acid value, saponification value, iodine volume, peroxide value, ethereal value. According to the results of the conducted studies of laboratory samples, the acid value is in the range of 0.612-0.69, the average result of the indicator is 0.633 with a relative error of ± 2.82 . The limits of the saponification value index are 150.0-154.0, with an average of $152.0 \pm 1.29\%$. The peroxide value is in the range of 0.195-0.203, the average result of the indicator is $0.199 \pm 1.73\%$. The iodine value is in the range of 1.14-1.64, the average result of the indicator is $1.35 \pm 1.33\%$. The ether value is in the range of 151.38, which meets the requirements of the pharmacopoeia article. Thus, the study of numerical indicators proves that the quality of the obtained oil extract meets the requirements of the SP RK.

Keywords: Oil Extract; Numerical Indicators; *Artemisia Cina*.

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3. Aggarwal S. et al. An extract of *Artemisia dracunculoides* L. stimulates insulin secretion from β cells, activates AMPK and suppresses inflammation. // Journal of Ethnopharmacology. – 2015. - №170. - P. 98–100.
4. State Pharmacopoeia of the Republic of Kazakhstan. - Almaty: Publishing House "Zhibek Zholy", 2014. - Volume 1. – pp. 155-159.

Research of *S. Pratensis* L. Leaves and It's Chemical Composition. Microscopy. Qualitative Analysis of Flavonoids. TLC Analysis of Cinaroside.

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Poster: P128

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Abstract:

Background. Search for diagnostic signs of *S. pratensis* L. leaves and research of it's chemical composition. Methods. The object is dried leaves of meadow sage. Microscopy, qualitative reactions and thin-layer chromatography were used. Results. Microscopy showed the presence of a diacytic stomatal apparatus, simple and glandular hairs and glands. Qualitative reactions with aluminum chloride solution confirmed the presence of flavonoids. Chromatography revealed the presence of cinaroside. Conclusion. Meadow sage leaves are promising medicinal plant raw materials.

Keywords: *Salvia Pratensis* L.; Microscopy; Flavonoids; Cinaroside; TLC.

The Effect of Plant-Derived Extract (Pde) on the Phagocytic Activity of the Blood of Mice Induced by Mieloma

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Abstract:

The effect of PDE on the phagocytic activity of the blood of mice induced by myeloma was studied. Modeling of induced myeloma in mice was performed by a single intraperitoneal injection of 106 myeloma cells per mouse. PDE 10-2 mol/l was administered using a gastric tube for 3 weeks. After 3 weeks, the mice were noted for the progression of myeloma, determined by body weight gain, an increase in ascites volume and median life expectancy for 3 months. It was shown that after the course of PDE therapy, the absorption activity of neutrophils increased, and the indicators of metabolic activity reached the level of the control group of intact animals. An increase in the metabolic activity of neutrophils, accompanied by increased formation of reactive oxygen species, correlates with a decrease in the progression of induced myeloma in mice, which indicates a possible mechanism of antitumor action by initiating apoptosis.

Keywords: Myeloma; Pharmacology; Plant Extract.

Pharmacognostic Study of Various Raw Materials *Crambe Abyssinica* Hochst. Igzakova Z.I., Galiakhmetova E.Kh., Kudashkina N.V.

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Abstract:

Pharmacognostic study of various raw materials *Crambe abyssinica* Hochst. Igzakova Z.I., Galiakhmetova E.Kh., Kudashkina N.V. Plants of the genus *Crambe* in the cabbage family Brassicaceae are annual and perennial herbs or subshrubs with simple large leaves that may be glabrous or pubescent with simple hairs. The leaf blade is entire or dissected (pinnatifid or pinnate-lobed). The flowers are small in racemes. Petals are white, rarely golden yellow. The coenocarp fruit of 2 carpels is an indehiscent two-membered pod. The most famous representatives of the genus: seaside katran (*Crambe maritima* L.), Tatar katran (*Crambe tatarica* Sebeok.), Kochi katran (*Crambe Kotschyana* Boiss.), heart-leaved crambe (*Crambe cordifolia*), Spanish crambe (*Crambe Hispanica* L.) and Abyssinian crambe (*Crambe abyssinica* Hochst.). *Crambe Abyssinica* (katran, Abyssinian mustard) is a valuable oilseed crop that naturally occurs in the Mediterranean countries, in North Africa and in the mountains of Ethiopia. The seeds of *Crambe abyssinica* contain a large amount of semi-drying oil with a low iodine value (93-97) and a high content of erucic acid (up to 60%). *C. abyssinica* oil is used in medicine and perfumery - it is included in moisturizing and nourishing creams for the face and body, and other cosmetic products. It has a firming, healing, nourishing and moisturizing effect. Sulfur-containing compounds of representatives of cabbage - glucosinolates decomposing to isothiocyanates have antitumor properties. Sulforaphane, also contained in the oil, is involved in the normalization of blood pressure, strengthens the walls of blood vessels and is used in the prevention of cardiovascular diseases. Indole - 3 - carbinol affects the metabolism of estrogen in the human body. In the pharmacy assortment, you can find a combination of "indole - broccoli" to maintain women's health, to regulate blood sugar levels, and as an antioxidant that prevents early aging. Therefore, the study of Abyssinian crambe as a source of valuable compounds is relevant. The purpose of our study at this stage was to study the content of the main groups of biologically active substances. The fruits collected during fruiting; fruit meal after oil extraction; grass harvested during flowering and during fruiting; roots - during fruiting. Types of raw materials were harvested from an introduced species on the territory of the Republic of Bashkortostan. The study of the quantitative content of ascorbic acid and tannins in the studied raw materials was carried out by the titrimetric method (titrants solution of 2,6-dichlorophenolindophenolate sodium and potassium permanganate solution, respectively), polysaccharides - by the gravimetric method (precipitation with ethyl alcohol 95%), flavonoids (in terms of narutin) - by spectrophotometric method according to the State Pharmacopoeia XIV. Studies have shown that the highest content of ascorbic acid is observed in seed meal and is 0.60%, tannins - in fruits (1.71%), polysaccharides - in grass harvested during flowering (16%). When studying the spectral analysis of the alcohol extract of the herb *Crambe abyssinica*, it was found that the spectrum coincides with the spectrum of luteolin. Therefore, when quantifying the amount of flavonoids in the herb, the recalculation was carried out for luteolin. In conclusion, we can say that *Crambe abyssinica* raw materials are a source of biologically active substances (tannins, polysaccharides, ascorbic acid, flavonoids) and can be an object for more detailed pharmacognostic and pharmacological studies.

Keywords: *Crambe Abyssinica* Hochst.; Tannins; Titrimetric Method; Flavonoids; Polysaccharides; Brassicaceae.

Perspectives of Studying Coffee Leaves (Coffee Arabica L.)

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Poster: P131

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Abstract:

The bias towards drugs of synthetic origin is strongly developing in the world of the pharmaceutical industry now. The use of synthetic drugs (antibiotics, sulfonamides, antiviral drugs, anticoagulants, etc.) by the population has increased significantly in recent years in the world. This became especially noticeable during the period of the Covid 19 coronavirus infection pandemic. Taking the above drugs has, among other things, undesirable consequences for peoples health. It is necessary to expand the range of medicines using the raw material base of the Russian Federation, the CIS countries and the world as a whole. A possible solution to this problem is the introduction into practice of new types of medicinal plant raw materials of known plants and their more detailed study. Of great interest is such a widely known plant as coffee. Coffee is grown in 65 countries. Most coffee is produced in Brazil (which accounts for about 40% of world coffee production), Colombia, Vietnam, Indonesia, Mexico, India and Ethiopia. Arabica is the most common type of coffee. You can prepare a drink not only from the grains of coffee berries, but also from the leaves of the coffee tree.

Keywords: Pharmacognosy; Research; Coffee.

Synthesis and Characterization of Hyaluronic Acid- Functionalized Ph-Sensitive MOF (ZIF-8) for Delivery of Methotrexate in Rheumatoid Arthritis

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Abstract:

Rheumatoid arthritis is a systemic autoimmune disease leading to chronic joint inflammation and a significant reduction in patients' quality of life., the existing drugs are not completely and definitively effective in treating the disease. On the other hand, due to low bioavailability, current treatments require frequent administrations with high doses. Also, improper distribution of medicine in the body causes numerous side effects. Therefore, responsive and targeted drug delivery systems are progressing. Considering the acidic environment and also the overexpression of the CD44 receptors on the surface of the inflammatory macrophages, we prepared hyaluronic acid- modified nanocarrier to load methotrexate drug, which is the mainstay of rheumatoid arthritis treatment, into the ZIF-8 acid-sensitive nanocarrier (Metal organic framework), which has a porous and biocompatible structure, in order to deliver drugs more effectively in this disease. Methods: For the synthesis of ZIF-8 nanocarrier, 2-methylimidazole was used as a linker, and Zinc nitrate.6H₂O was used as the central metal. The loading of the methotrexate in the nanocarriers was investigated by one-step (in situ) method. Finally, to study targeted drug delivery for rheumatoid arthritis and control drug release, the nanocarrier was coated with hyaluronic acid. DLS, Zeta potential, FESEM, XRD, FTIR, and BET tests were carried on for analysis of nanoparticles characteristics. Drug loading and entrapment efficiency were measured using the UV-Vis method. Also, drug release from the coated and uncoated systems was measured in environments with different pH values. Results: Synthesis of ZIF-8 was confirmed with XRD, FTIR and FESEM. Then methotrexate was loaded successfully with the 68 % Entrapment efficiency and 30% loading capacity. Hyaluronic acid modified MTX@ZIF-8 was made by immersing the nanoparticles in an aqueous solution of hyaluronic acid. The hydrodynamic diameters of ZIF-8, MTX@ZIF-8, MTX@ZIF-8 /HA were 170, 178.1, and 192.6 nm, respectively, and the zeta potentials were 24, 17.3, and -32.6, respectively. Also, the surface area of MTX@ZIF-8 nanoparticles was 950.25 m²/g-1, while it was 1620.30 m²/g-1 for ZIF-8. This decrease indicates the successful loading of the drug. Also, ZIF-8 nanoparticles had high crystallinity which did not change even after drug loading. The drug release in 2 first hours was 15.716% and 29.961% for MTX@ZIF-8/HA and 27.044% and 54.515% for MTX@ZIF-8 in pH=7.4 and pH=5 respectively. And in 53 hours it was 58.882% and 94.446% for MTX@ZIF-8/HA and 68.808% and 100% for MTX@ZIF-8 in pH=7.4 and pH=5 respectively. Conclusion: The fabricated ZIF-8 had appropriate size, PDI, crystallinity, specific surface area, and correct morphology as well as relatively good %entrapment efficiency values. The drug release in acidic environment that exists in the inflammatory tissue was faster. Thereafter the nanoparticles were coated with hyaluronic acid to target the CD44 receptors, which was confirmed by measuring zeta potential and FTIR. Also, after coating, the drug release of coated nanoparticles was slower especially at physiological pH. In the continuation of the work, it is suggested that the coating of the particles with hyaluronic acid is confirmed by the TEM test, and also the toxicity, and in vivo tests are also investigated.

Keywords: Metal-organic framework; ZIF-8; targeted drug delivery; methotrexate; rheumatoid arthritis; Hyaluronic acid.

Prediction of Solubility Class in Biopharmaceutics Classification System Title

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Abstract:

Abstract Introduction: The Biopharmaceutics Classification System (BCS) has turned out to be commonly accepted in academia, industry, and regulatory world. Biopharmaceutics Drug Disposition Classification System (BDDCS) is a modification of BCS which is a four-class system based on solubility and metabolism. This system assigns the role of carriers in pharmacokinetics and their interaction with metabolizing enzymes (1, 2). Drugs are classified into four groups in terms of the extent of permeability (BCS) or metabolism (BDDCS) and solubility, high and low, based on BDDCS (3). In order to predict classes, structural parameters of drugs were used to create classification-based models. Against metabolism and permeability, the previous models cannot predict solubility class with good accuracy (4). Therefore, the aim of this study is to improve the capability of the models for estimating solubility class. **Material and methods:** Firstly, drugs' BDDCS data were collected through the literature, then, the structural descriptors including Abraham solvation parameters, distribution coefficient (log D) and octanol–water partition coefficient (log P) were computed by ACD/Labs software. Later, data were divided into two portions including training and test. The training set was applied to develop the models based on structural parameters by logistic regression. **Results:** The developed models based on Abraham solvation parameters and log P and log D could predict the class of solubility with good accuracy. **Discussion:** The outcomes of this research revealed that the accuracy for the prediction of the class of solubility was improved after the inclusion of drugs ionization in biological pHs, in addition to Abraham solvation parameters and log P. Hence, the developed classification models can estimate solubility class with satisfactory accuracy. **Conclusions:** The class of solubility can be estimated with high accuracy with the aid of the applied structural descriptors of drugs.

Keywords: Solubility; Prediction; Model; Physicochemical; Accuracy.

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Computational Approaches for Estimating Renal Clearance Type of Drugs Using Their Structural Descriptors

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Abstract:

The excretion of drugs and their metabolites by kidneys plays a vital role in drug elimination, especially for drugs with negligible metabolic, and biliary clearances [1]. Renal excretion is a net result of several processes, which are active secretion, glomerular filtration, and tubular reabsorption [2]. In-vivo methods to determine the type of renal clearance, necessitates animal and human data, spending more time with huge amount of money while nowadays, computational approaches are of interest scientists to reduce the sources. The aim of this study is to develop in-silico models to find out the relationship between the type of renal clearance, and structural parameters of drugs. Methods: A dataset of 391 drugs with their human renal clearance was used in this study. Drugs with $CL_{rfu} \times GFR$ and $CL_{rfu} \times GFR$ were divided into reabsorption and secretion, respectively. One hundred seventy-four chemical descriptors were calculated by VolSurf, ACD/Labs and data warrior to establish interpretable in-silico models to predict the type of renal clearance. Before the selection of descriptors for each model, the bivariate correlation was done and collinear descriptors ($R^2 > 0.8$) were not used together in a model. Results and discussion: The results of this study indicate that $\log D_{7.4}$ and the number of hydrogen bond donors, as well as available uncharged species (AUS_{7.4}), are the most effective descriptors to establish mechanistic models for predicting renal clearance type. Drugs with high $\log D_{7.4}$ and AUS_{7.4} values, which are considered as hydrophobic drugs are more permeable to biological cells and tend to be eliminated via reabsorption rather than secretion. In addition, ability to form hydrogen bonds is one of the factors that could make a compound more hydrophilic. Drugs with higher hydrogen bonding ability are more likely to be secreted. The classification models were established with a level of accuracy of more than 75%. Conclusion: In this study, several computational models were obtained in order to estimate the type renal clearance. Developed models from this study could be useful to estimate drug's renal clearance type with an acceptable error.

Keywords: Clearance; Prediction; Renal.

Preparation of Reduction and Radiation-Sensitive Starch-Based Magnetic Hydrogel Containing Doxorubicin and Investigating the Possibility of its Application

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Abstract:

Today, cancer is considered as one of the most important causes of human mortality and its treatment is faced with many problems, therefore, the development of new targeted and more efficient drug delivery systems can lead to better treatment and less side effects. One of these new methods is the production of stimulus-sensitive hydrogels. In order to achieve this goal, in this study, a hydrogel sensitive to reduction and radiation containing manganese dioxide nanoparticles was synthesized based on starch and was used for the targeted drug delivery of doxorubicin as well as chemotherapy/radiotherapy. First, starch was carboxylated in a base medium using 2-chloroacetic acid during a substitution reaction. Manganese dioxide nanoparticles were synthesized using its acetate salt in a strong alkaline environment and the surface of the synthesized nanoparticles was modified using trimethoxysilylpropylamine. The chemical structure and physical and chemical properties of the synthesized hydrogel were analyzed by different methods. Finally, the synthesized hydrogel was physically loaded with the anticancer drug doxorubicin. Biocompatibility of synthesized hydrogel was studied by MTT test method on MCF-7 cell line (breast cancer cells). In addition, the toxicity of hydrogel loaded with doxorubicin on MCF-7 cell line was studied by chemotherapy alone and chemotherapy/radiotherapy (with 6 MV photon beam) by MTT method. Result: Examination of toxicity tests showed that chemotherapy/radiotherapy was more effective than chemotherapy alone, and therefore the designed system has good potential as a targeted drug delivery system for cancer chemotherapy and radiation therapy. The design and development of hydrogels based on natural and stimuli-responsive polymers, as new drug delivery systems, can be an important issue in cancer treatment due to negligible side effects, targeted drug release and improvement of clinical results.

Keywords: Cancer; Stimuli-sensitive hydrogel; MnO₂ nanoparticles; Doxorubicin; Chemotherapy/radiotherapy

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Metal Nanoparticles: A Promising Solution to Overcome Multidrug-resistant Bacteria

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Abstract:

The usage of Antibiotics is expanding as a consequence of a number of variables, including aging of the population, an increase in infections, and a rise in the number of chronic illnesses that need antibiotic treatment. People have been using antibiotics excessively and recklessly, that has resulted in the increase of bacteria resistance to the drugs which are currently accessible, in addition to the selective expansion of other germs. This has contributed to the spread of resistance genes widely in the environment. Therefore, efforts are being done to create novel strategies to tackle resistant bacteria. One of the most efficient strategies is the application of nanoparticles (NPs). Nanoparticles can enhance stability, solubility, penetration and antibacterial properties of drugs while protecting drugs from enzymatic degradation. They also obtain a prolonged drug release, half-life and bioavailability which leads in lower effective therapeutic dosage and therefore fewer side effects. **Methods and Results:** In this study we designed an approach to combat MDR by utilizing inorganic metal NPs, including AgNPs, AuNPs and metal oxides such as ZnO. The results are as below: silver nanoparticles (AgNPs): The most promising approach among all of the inorganic NPs for treating bacterial infections are silver nanoparticles (AgNPs). Reactive oxygen species (ROS) synthesis, suppression of cell wall formation, and ribosome instability are some of the mechanisms by which AgNPs cause cell death. Gold nanoparticles (Au-NPs): antibacterial mechanisms of Au-NPs consist of: respiratory chain disruption, decreased ATPase activity, and reduced tRNA binding to ribosomal subunit. Zinc oxide nanoparticles: ZnO NPs antibacterial functions include producing ROS, preventing the formation of biofilms, degrading proteins and lipids and modifying the permeability of bacterial cell membrane. Lipopolysaccharide (LPS) is notably located on Gram-negative bacteria, whereas Teichoic acid appears in Gram-positive bacteria. LPS and phospholipid in Gram-negative bacteria create a barrier against nanoparticle penetration and it has a selective permeability, whilst teichoic acid and peptidoglycan along with numerous pores in Gram-positive bacteria allow entrance of foreign particles, including nanoparticles. Consequently, nanoparticles are found to be more efficient against Gram-positive bacteria than Gram-negative bacteria. Therefore, due to metal NPs' extremely small size and large surface area, they offer enormous therapeutic potential and are effective against a wide variety of conditions while being generally nontoxic and harmless to mammalian cells. **Conclusion:** These clinical difficulties underscore the urgent need for novel and efficient antibacterial methods. Proteoglycans are primarily responsible for the attachment of nanoparticles to bacterial membranes, which causes the membrane to rupture or become more permeable. As a result, the nanoparticles can penetrate the cell and interact with DNA and enzymes. Altogether, NPs provide a promising alternative platform to current treatments for solving the current issue that society faces. Future research is required for nanotechnologies to be used more widely for treatment of MDR pathogens.

Keywords: nanoparticles; multidrug resistance; antimicrobial resistance; Bacteria; metal nanoparticles; nanotechnology.

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In Silico Evaluation of Crocin-Phospholipid Complex Using Computational Molecular Modeling and Simulation

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Abstract:

In addition to discovering new active molecules, computer-aided molecular modeling and simulation studies proved to be a valuable tool for conformational analysis and prediction of stability on a molecular level (1, 2). Crocin, a water-soluble carotenoid isolated from saffron (*Crocus sativus* L.), has shown medicinal properties such as anti-inflammatory, antioxidant, and anti-tumorigenic in various animal studies. However, poor stability and low lipophilicity have restricted its pharmaceutical applications (3). Phospholipid complexation represents a promising approach to improve stability and enhance the bioavailability of natural substances. Hydrogen bonding and hydrophobic interaction have been reported between the drug and phospholipid to form a complex (4, 5). Methods: Molecular modeling studies were carried out using Maestro 10.2 (Schrödinger LLC). Initially, the chemical structures of crocin and phospholipid (egg phosphatidylcholine) were obtained from PubChem as SDF files in 2D. Then, the 2D structures were converted to 3D, and energy was minimized under the OPLS3 force field using the ligand preparation task. Thereafter, the conformational analysis of the crocin-phospholipid complex was carried out using the ligand-receptor complex task under the OPLS3 force field in vacuum, water, octanol, and chloroform. Both crocin and phospholipid were allowed to be flexible. Finally, detailed analysis of the crocin-phospholipid interactions and visualization were accomplished with the help of Pymol® software version 2.1.0. Results: The calculated potential energies of the crocin-phospholipid complex in water, octanol, chloroform, and vacuum were -234.473, -209.080, -102.294, and 113.872 kJ/mol, respectively. It can be concluded that the crocin-phospholipid complex has the most stable conformation in water. The results obtained from Pymol® also indicated that van der Waals forces and hydrophobic interactions may establish between the crocins hydrophobic portion and phospholipids two hydrophobic arms during complexation. The computer-aided molecular modeling and simulation study was a rapid and efficient tool to show the possibility of crocin-phospholipid complex formation and its stability in different media.

Keywords: crocin; phospholipid complex; molecular modeling; Schrödinger; energy minimization.

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Methotrexate and Tamoxifen-Loaded Magnetic Nanoparticles: Efficacy and Cytotoxicity

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Abstract:

Nanotechnology is gaining significant attention worldwide for cancer treatment. Although methotrexate (MTX) and tamoxifen (TMX) are administered against breast cancers, their role has been limited due to their dose-dependent complications and low bioavailability. In the last decades, synthesis of magnetic nanoparticles (MNPs) has shown great potential for the formulation of drug delivery systems (DDS). Objective: In this study, to improve drug delivery to the target tissue, reduce drug cytotoxicity, and increase its efficiency, MTX and TMX-loaded MNPs were prepared and their efficacy and hepatotoxicity were evaluated. We used MCF-7 cells to investigate the efficacy of MTX and TMX-loaded MNPs and extracted normal rat liver cells to evaluate its cytotoxicity using the MTT assay and Real-Time PCR. All statistical analysis was performed using SPSS 17 and One-Way ANOVA Test.

Keywords: Nanomedicine; Drug Delivery System; Magnetic Nanoparticles; Breast Neoplasms; MCF-7 Cells; Hepatotoxicity.

Formulation and Accelerated Stability Study of a Vanishing Cream Containing Propolis Extract

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Abstract:

Propolis, referred to as bee glue, is a mixture of plant buds, bee saliva, and wax produced by honey bees with the purpose of hive protection (1, 2). Propolis is a well-known natural agent, which has been investigated to comprise more than 300 compounds and has a brief application in traditional to modern medicine (3). Propolis is also considered an effective active ingredient in cosmeceutical products thanks to its antibacterial, anti-inflammatory, antioxidant, and rejuvenating properties (4). Regarding the high trend toward natural cosmeceutical products and its expanding market (5), developing a stable formulation containing Propolis is an influential attempt in the skin care industry. Material and Method Crude Propolis was purchased from Khoy, Azerbaijan province, Iran. Freeze Propolis was crushed to a fine powder, and a hydroalcoholic extract of Propolis was prepared using ultra-sonication. The condensed extract was obtained following solvent evaporation. The total phenolic content of the extract was determined based on Galic acid content through UV-spectroscopy using Folin-Ciocalteu. A vanishing cream was well designed based on stearic acid and triethanolamine reaction, optimized by further excipients, and nourished by adding 5% w/w Propolis extract and almond oil. The accelerated stability study was conducted on the final formulation for 3months, and the phenolic content available in the cream was determined periodically based on UV spectroscopy. Results The phenolic content of the crude Propolis was determined based on Galic acid. The final formulation of the cream revealed desired texture, homogeneity, and after-feel. The pH of the formulation was estimated to be 5.8 by a pH meter. The HLB of the cream was calculated to be 13 and combined with Sudan color; microscopic observation confirmed the emulsion to be oil in water. In periodic examination physical properties of the cream remained stable, and the total phenolic content of the formulation was almost the same as crude Propolis based on UV-spectroscopy results, which exhibit the chemical stability of the cream. discussion Regarding the high trend of natural cosmeceutical products, taking advantage of potent natural active ingredients is essential to promote the efficacy of previous products. In this respect, Propolis has been considered beneficial in skin care products. Hence, we developed a topical formulation containing Propolis extract, and interestingly the physicochemical evaluation results indicated the formulation stability in addition to desired properties according to consumer demand. Conclusion The created formulation revealed proper physicochemical properties, and according to the previous pharmacological assessments, it is a promising product for skin care. Further experiments may be needed to upgrade the formulation by adding more natural ingredients.

Keywords: propolis; vanishing cream; formulation; stability study.

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Optimization of Pegylation Condition of Recombinant Interferon Beta-1a

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Poster: P140

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Abstract:

Interferon beta 1a is a single-chain glycosylated human protein. It has 166 amino acids, and its molecular weight is 22.5 kDa. This protein is a type I interferon that inhibits the proliferation and activation of T- lymphocytes to control inflammation. Recombinant interferon beta 1a as a medicine in patients suffering from multiple sclerosis (MS), because of its higher clearance rate from the body, is needed to inject one other day in a week. in order to overcome the side effects of daily injections of this biopharmaceutical its PEGylation has done. PEGylation is the covalent attachment of activated polyethylene glycol (PEG) to a biomolecule which can cause a significant increase in the size of the PEGylated biomolecule, consequently decreasing its body clearance. In this study, we optimized the condition of site-specific PEGylation of interferon beta 1a. To achieve this aim, we received API (active product ingredient) of this biopharmaceutical from Cinnagen company, and PEGylated it using 20 kDa linear mPEG aldehyde at N-terminal under various conditions of reaction pH, Temperature, PEG to protein molar ratio, and reaction time. The reaction mixture is analyzed using sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) technique on 10% gel and silver staining method applied to stain gels. According to the obtained data, higher and cost-benefit PEGylation yield was achieved at PEG to protein molar ratio of 4, reaction temperature of 15°C, reaction pH of 4, and a time of 10 hours. As the reaction volume was small (0.5 to 1 mL) and the reaction has done in 2 mL micro tubes, to confirm the achieved data and to have the scale able PEGylation method, we will repeat the PEGylation reaction in higher in a 15 mL falcon tube.

Keywords: PEGylation; Interferon beta 1a; Site specific PEGylation.

Reference:

10.1021/bi991631c, 10.1089/jir.2010.0092, 10.1016/ S1474-4422(14)70068-7, 10.2165/00003088-200140070-00005

Photoacoustic and Ultrasound-Based Nanotheranostics: A review

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21-23 February 2023

Poster: P141

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Abstract:

Ultrasound (sonography: US) and photoacoustic imaging (PAI) are two desirable medical imaging techniques due to their safety and capability to provide real-time images from deep tissues. In the former, the high frequency sound waves (>20 kHz) and US (Ultrasound) are emitted inside the body and the reflected waves from the internal organs create the images. For the latter, non-ionizing laser pulses are sent into body and part of the energy will be absorbed and turned into heat, leading to ultrasonic emissions. Then, the images can be created via the reflected ultrasonic waves. The emergence of gas-filled microbubbles and small molecule organic dyes as ultrasound and PAI contrast agents accelerates their applications in diseases diagnosis [1, 2]. The microbubble-based ultrasound imaging agents can also carry the genes, chemo-toxic drugs and photosensitizers and release them under high pressure amplitude leading to their therapeutic application [1]. In this review we focus on the nanoparticle-based contrast agents used in US and PAI with diagnostic and therapeutic functions at the same time called “theranostics”. These platforms are able to selectively accumulate into targets (e.g., tumors) by enhanced permeability and retention (EPR) effect and release their therapeutic or diagnostic cargoes. For metallic nanoparticles as Au NPs and etc., the nanostructure itself plays dual role in diagnosis and treatment via absorption of the light and its conversion into the sound required for PAI or the heat which can destroy the tumors (photothermal therapy) [3]. There is also phthalocyanine/naphthalocyanine-based nanoparticles served as PAI agents which are theranostics [4]. This review aims to describe the nanoparticles used as exogenous contrast agents in US and PAI being of therapeutic effects, simultaneously.

Keywords: photoacoustic imaging; theranostic; Ultrasound.

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Preparation and Characterization of Chitosan Nanofibers Containing Pomegranate Flower Extract

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Abstract:

Pomegranate (*Punica granatum* L.) flower extract (PFE), is commonly used in traditional medicine for bleeding and inflammation. The chemical components of pomegranate flowers include polyphenols, flavonoids, and saponins (1). Its main phenolic active ingredient is gallic acid, which is a natural antioxidant (2). It has been proven that PFE possesses many therapeutic values, including antioxidant, astringent, and anti-inflammatory effects (3). Novel topical drug delivery systems, such as nanofibers and hydrogels could be manufactured for localized delivery of PFE (4). Nanofibers are suitable systems for the local delivery of PFE due to their characteristics, including high surface area, porosity, and permeability. Chitosan (CS) is a natural, non-toxic polymer with high biodegradability and biocompatibility, and antibacterial effects. Pure CS cannot be electrospun into nanofibers with favorable nanostructure due to its low spinning ability (5). Therefore, in this study, gelatin (GEL) was blended with CS to prepare electrospun nanofibers with the desired physical properties. In order to prepare PFE, dried petals of pomegranate flower were added to water at room temperature. After 24 hours, the flowers were filtered and the solution was heated at 90 °C for 24 hours. The total flavonoid content of the PFE was measured using quercetin as the standard flavonoid. To prepare the nanofiber solution, 30 w/w% GEL and 3 w/w% CS solutions in acetic acid were blended at 25:75, 50:50, and 75:25 weight ratios. Pomegranate flower extract was subsequently added with extract: polymer weight ratio of 1:8. The nanofibers with GEL to CS ratio of 25:75 showed beads and particles. However, other ratios resulted in beadless nanofibers. We chose the formulation with the highest CS concentration, CS50-GEL50, as the optimum formulation for future tests. The release profile of PFE was also studied, which showed a controlled drug release from the nanofibers.

Keywords: Chitosan; Nanofiber; Pomegranate flower extract.

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Preparation and Characterization of Chitosan-based Hydrogels Containing Chlorhexidine for Root Canal Irrigation

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Abstract:

Root canal irrigation is primarily performed to remove the microbial community in the dental root canal. The irrigation is usually performed using various irrigation solutions, such as chlorhexidine and hypochlorite (1). Chlorhexidine is a broad-spectrum antibacterial agent, which can effectively remove the bacterial strains present in the infected root canals (2). Chlorhexidine could be delivered locally using novel drug delivery systems. Hydrogels are three-dimensional structures that are biocompatible, absorbable, and non-toxic. Therefore, they could increase the efficacy of the treatment (3). Chitosan is a natural polymer with acceptable mechanical stability, biodegradability, and biocompatibility as well as antimicrobial properties (4) which is especially appropriate for root canal delivery of antimicrobial agents. Methods: Various in situ gel chlorhexidine formulations were prepared using 16-20 w/v% β -glycerophosphate (β GP) and 1.6-2 w/v% chitosan. To prepare the formulation, chitosan and β GP powders were dissolved in acetic acid and water, respectively. The drug was added to the chitosan solution. Then, the β GP was dropwise added to the CS solution at 4°C. The gelation time and temperature of each hydrogel were recorded. Results: It seems that the formulation characteristics were affected by the concentration of β GP, CS, and chlorhexidine. Moreover, mixing sequence and duration may influence gelation time and temperature. The gelation temperature ranged between 30°C to 40°C. The gelation time varied from 1 min to 12 min. Conclusions: Chitosan-based chlorhexidine hydrogel was successfully prepared for root canal irrigation.

Keywords: Hydrogel; Chlorhexidine; Root canal irrigation; Chitosan.

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Preparation of Tragopogon Graminifolius-Loaded Electrolyzed Electrospun Nanofibers to Improve its Wound Healing Activity in a Rat model of skin Scar

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Poster: P144

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Abstract:

Growing studies are trying to provide novel wound healing agents with fewer side effects. Polyvinyl alcohol/polyethylene oxide/chitosan nanofibers are effective in wound healing due to their stimulation of collagen production. Among the herbal agents with fewer side effects, Sheng (Tragopogon graminifolius) is one of the effective plants in the treatment of various skin injuries. In the current study, a nanofibers of polyvinyl alcohol/polyethylene oxide/chitosan containing sheng has been evaluated in the wound healing process. Materials and Methods: Synthesized nanofibers from polyvinyl alcohol, polyethylene oxide, and chitosan were prepared by the electrospinning method and confirmed by SEM and FTIR test. The release tests of nanofibers were carried out by UV visible method in various time intervals and last up to 72 hours. Animal testing was performed by creating wounds on Wistar rats and measuring the wound area at days 0, 3, 7, 10, and 14. On the 15th day, the seum levels of nitric oxide and catalase were measured. Additionally, wound tissue was removed and histological studies were performed. Results and Discussion: polyvinyl alcohol/polyethylene oxide/chitosan nanofibers containing 0.8 g of chitosan, 1.2 g of polyvinyl alcohol and 0.3 g of polyethylene oxide along with 50% Tragopogon graminifolius extract at 17 kV were selected due to related suitable morphology and more uniform quality. Polyvinyl alcohol/polyethylene oxide/chitosan nanofibers containing 50% Sheng extract showed promising effectects in wound size, histopathological results and oxidative stress mediators (e.g., nitric oxide and catalase) in Wistar rats.

Keywords: Tragopogon graminifolius; Wound, Rat; Polyethylene oxide; Polyvinyl alcohol; Electrospinning.

Synthesis and Characterization of a Ph-Responsive Nanoparticle Coated with Hyaluronic Acid for Methotrexate Delivery in Rheumatoid Arthritis

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Poster: P145

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Abstract:

Methotrexate, as the drug of choice in treatment of rheumatoid arthritis (RA), is the reason for different adverse effects and the presence of the drug in areas of the body that are not involved in the disease, may worsen the side effects. To address this issue, novel drug delivery systems are utilized to ensure targeted delivery and minimal side effects. Metal-organic frameworks (MOFs) are one of the nanocarriers used for this purpose. These carriers have high porosity and capacity for drug loading. A kind of MOF that due to being acid-responsive, can be used in the acidic environment of the joints in RA, is MIL-100(Fe) and the goal of this research is synthesis, characterization, and in vitro evaluation of this nanoparticle, in RA drug delivery. Coating the MOF can also assist in targeted delivery of the disease. Methods: Trimesic acid (BTC or benzene tricarboxylic acid) and FeCl₃·6H₂O were used alongside methotrexate for MOF preparation. BTC was the organic ligand used to support the iron metal in constructing the porous MOF structure. Chitosan, 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC), and hyaluronic acid were also applied for MOF coating. The role of EDC was to help form the amide bond between the amine functional groups from chitosan and the carboxylic acid groups of hyaluronic acid. Drug loading and release of the nanoparticle were evaluated with, and without coating; UV-Vis-derived calibration curves were employed to calculate the drug concentration of the post-centrifugation supernatant and assess these two parameters. Some other tests were also implemented such as; UV-Vis and FT-IR tests for methotrexate characterization, XRD, BET, FESEM, FT-IR, and zeta potential tests for MIL-100(Fe) characterization, and FT-IR and zeta potential tests for the coated MOF evaluation and as a means to show the success of the coating process. Results: MOF synthesized via microwave-assisted route, was initially loaded with methotrexate, then coated with chitosan, and lastly, the chitosan coating was attached to hyaluronic acid via EDC. Other synthesis routes were also tested; hydrothermal, mechanochemical, mechanochemical, room temperature synthesis with water, room temperature synthesis with organic solvent, and reflux methods were tried to achieve optimum MOF with small size and good crystallinity. BET test didn't show enough surface area but the adsorption-desorption graph presented type IV isotherm with hysteresis loop indicating porosity. The needle-like MOF was approximately 275.371±39.799 nm in length, and 44.758±3.276 nm in width. The coating around the nanoparticle, prevented the burst-release of methotrexate. The drug delivery system was stable in water for 7 days. For the coated MOF, EE% and LC% were around 93% and 12.6%, respectively. Conclusion: MIL-100(Fe) nanocarrier coated with hyaluronic acid and chitosan was found efficient for targeted delivery of methotrexate in rheumatoid arthritis. To further continue this work, it is suggested that the coating of the particles is confirmed by TEM, and cell cytotoxicity, drug uptake, and cytokine release tests are performed on RAW264.7 cell lines for in vitro evaluation. Animal studies, application of photodynamic therapy, and utilization of MRI is suggested for future works.

Keywords: rheumatoid arthritis; methotrexate; metal-organic framework; responsive; targeted delivery; novel drug delivery systems.

Investigating the Protective Effect of Rutin Loaded in Chitosan/Tripolyphosphate Nanoparticles in an Animal Model of Rheumatoid Arthritis

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21-23 February 2023

Poster: P146

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Abstract:

Rutin is a flavon glycoside known as an anti-inflammatory and antioxidant compound. Rheumatoid arthritis is an autoimmune inflammatory disease that leads to joint destruction and disability in patients. The purpose of this study is to prepare a nanoformulation containing rutin with the aim of increasing its bioavailability, solubility and improving its effectiveness in order to investigate the neuroprotective effect of this compound in an animal model of rheumatoid arthritis induced by Freund's complete adjuvant. Materials and methods: In this study, in order to investigate the antioxidant effects and the efficiency of the rutin drug delivery system, the induction model of rheumatoid arthritis was used by Freund's complete adjuvant injection. After the induction of rheumatoid arthritis in each group, the effect of injection alone and with an effective dose of nanoparticles containing rutin, rutin, and compared with the prednisolone as the positive control group have been evaluated using open field, inclined plane, Von Fery, hot plate, and acetone drop besides measurement of serum levels of nitric oxide, glutathione and catalase and finally histopathology studies. Results: The results showed that the injection of Freund's complete adjuvant compared to the control group that received distilled water increased the immobility time of the rats in behavioral tests that received nanoparticles containing rutin, especially at a dose of 30 mg/kg. This significantly reduced the immobility in the mentioned tests. In addition, the induction of rheumatoid arthritis significantly increased the amount of nitric oxide and significantly decreased between glutathione and catalase, while the group receiving nanoparticles containing rutin and prednisolone reversed these effects. Also, this rutin drug delivery system in the joint plays a significant role in the improvement of histopathological symptoms in a dose-dependent manner and is comparable to prednisolone. Oxidative stress impacts the immune system by diminishing the function of the antioxidant levels and eventually leads to autoimmune diseases, including rheumatoid arthritis (RA). The attending analysis investigated the antioxidant effect of polyphenol rutin nano formula to improve the bioavailability, solubility, delivery, and targeted release of this compound in the intestine, which was also dose-dependently confirmed. According to the results, the administration of nanoparticles containing rutin leads to a decrease in the serum level of nitric oxide and an increase in the serum level of glutathione and catalase. Considering the improvement of behavioral and tissue symptoms and the relative reduction of the level of inflammatory cytokines, nanoparticles containing rutin can be proposed as a suitable approach in the control of rheumatoid arthritis disease.

Keywords: Freund's complete adjuvant; rheumatoid arthritis; Rutin nanoparticles.

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Preparation and Evaluation Eye Drop Formulation Based on Hyaluronic Acid and Vitamin B12

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Abstract:

Introduction Dry eye disease is a common age-related disease in the world. Vitamin B12 is an essential factor in maintaining eye health and has antioxidant properties that protect the surface of the eye from damage caused by harmful factors such as reactive oxygen species. Hyaluronic acid polymer is also very similar to natural eye tears with its biocompatibility and physical properties and this polymer is one of the important components of the extracellular matrix. Due to the lack of formulations containing the combination of vitamin B12 and hyaluronic acid in the country and appropriate effects of these two compounds for dry eyes, we decided to formulate and analyze the stability of Eye drop formulation Based on Hyaluronic acid and vitamin B12. **Materials and methods** First, the formulation of hyaluronic acid and vitamin B12 solution with borate buffer was prepared and the stability of vitamin B12 were evaluated. In the following, the physicochemical properties of the prepared formulations were evaluated and sterile ophthalmic solution was prepared from the selected formulations under aseptic conditions. Finally, by choosing the final formulation, accelerated stability was done. The results of the tests were analyzed using Graphpad prism software. **Results** Accelerated studies after six months showed that the amount of vitamin B12 and its UV absorption did not decrease, and the physicochemical properties such as solution pH, color and viscosity did not change. **Conclusion** In conclusion, according to the results, this formulation could be a good candidate for industrial production and long-term studies are recommended.

Keywords: Vitamin B12; Dry eye disease; Hyaluronic acid.

Exosome-Based Drug Delivery in Breast Cancer

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Abstract:

Breast cancer (BC) is the second most common cancer in the world. The common methods of treating this disease are: hormone therapy, radiotherapy, chemotherapy, surgery and immunotherapy. Chemotherapy is the most widely utilized treatment method, which has side effects such as hair loss, vomiting, nephrotoxicity and neurotoxicity. Therefore, new methods of drug delivery based on nano platforms in order to prevent systemic toxicity and targeted transfer of drugs to the tumor site is a new approach that has attracted the attention of researchers. Exosomes are potential biological nanovesicles that consist of two lipid layers and have attractive advantages in drug delivery and transport of medicinal agents in breast tumor treatment. They are 30-100 nm in sizes, and are derived from biological fluids such as blood, saliva, urine, pancreatic juice, bile, and cerebrospinal fluid. Their advantages include biocompatibility, biodegradability and non-immunogenicity. Compared to artificial carriers, exosomes have a controllable and long lifespan, small size, low toxicity, natural targeting ability, and encapsulation of various bioactive molecules. They can be isolated by several methods, including ultracentrifugation, precipitation, immunoaffinity, size-exclusion chromatography, and ultrafiltration. After the isolation of exosomes, drugs or bioactive molecules can be loaded by one of the methods of electroporation, sonication, incubation, and extrusion. Exosomes derived from mesenchymal stem cells were isolated by centrifugation and loaded with paclitaxel drug with the incubation method. In NODscid mice, metastatic MDA-hyb1 breast tumors were induced and then intravenously injection of MSC-derived exosomes loaded with paclitaxel resulted in 60% tumor reduction. Immature dendritic cells were utilized to isolate exosomes by centrifugation, then the drug doxorubicin (Dox) was loaded by electroporation. Breast cancer was induced in mice by transplantation of human breast cancer cells (MDA-MB-231). Subsequently, Dox-exosome was intravenously injected into the tumor tissue, which reduced tumor growth. Therefore, drug delivery cancer cells using exosomes is a promising therapeutic approach to treat and reduce their side effects.

Keywords: drug delivery; Exosome; Breast Cancer; paclitaxel.

Synthesis of CuO-Rgo-Mwcnts Nanostructure and its Use in Construction of a Sensitive Biosensor for Metformin Determination

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Poster: P149

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Abstract:

In part two, a glassy carbon electrode was modified by copper oxide/reduced graphene oxide/multiwall carbon nanotubes (CuO rGO-MWCNTs) and used for electrochemical determination of low-level metformin using differential pulse voltammetric (DPV) method. The prepared electrode showed high stability in the composite film, short response time, good reproducibility and an excellent selectivity. This biosensor has linear concentration ranges from 0.01 to 100 μ M, and the limit of detection of 0.95 μ M.

Keywords: Biosensor; Nanocomposite; Cyclic voltametry; Electrochemical detection; Metformin.

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Assessment of the Quality of the Data Provided on Nonsteroidal Anti-Inflammatory Drugs in Kyrgyz Republic

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21-23 February 2023

Poster: P150

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Abstract:

The article reviewed the results of the data obtained on the availability of information regarding nonsteroidal anti-inflammatory drugs (NSAIDs), which the buyer receives from a pharmacist in a pharmacy. The study was conducted using an anonymous, non-repetitive online survey, which involved 620 people. During the survey, it was found out that the majority of respondents (35.9%) receive information from a pharmacist and buy NSAIDs according to their recommendations, while 33.1% purchase certain medications according to a doctor's prescription. 89.7% of respondents focus their attention on the effectiveness of the drug. Also in the questionnaire, 69.4% indicated the usefulness of advertisements that provide information about drugs. It is noted that 52.2% of pharmacists recommend drugs from certain pharmaceutical manufacturers. Half of the respondents are satisfied with the quality of the information provided by the pharmacist. It was noted that the lack of proper time and low qualification of pharmacists became essential in the insufficient level of counseling.

Keywords: NSAIDs; Anonymous Non-Repeated Survey; Drug Buyers; Pharmacist Qualification.

Development of Technologies for Waste-Free Processing of Leaves of *Heracleum Sosnovskyi*

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21-23 February 2023

Poster: P151

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Abstract:

One of the important problems of modern pharmacy is the search for new types of medicinal plant raw materials and have a waste-free production. The analysis of the scientific literature showed the presence of a large number of articles that proved the presence of coumarins in the *Heracleum Sosnovskyi* M., as well as the prospects of using this raw material for the treatment of psoriasis, nest baldness and baldness. The analysis of external signs of leaves of *Heracleum Sosnovskyi* M. was carried out. In the course of this study, morphological-anatomical and microdiagnostic analyses of the leaves of *Heracleum Sosnovskyi* M., which were harvested in the Moscow region in the Pushkin district, were carried out. In the course of qualitative reactions with samples of raw materials and water-alcohol extracts obtained on its basis, the identity of the composition of the main groups of biologically active substances represented by flavonoids, coumarins, tannins and substances, phenolcarbonates and acids was established. The composition of the coumarin fraction was determined using the thin-layer chromatography method. In the course of the study, a sample of the powder of the leaves of the *Heracleum Sosnovskyi* M. was obtained, which is a possible waste of pharmaceutical production to be disposed of, and their adsorption capacity was evaluated in comparison with similar indicators of traditional enterosorbents – the preparation "Polyphepan" and microcrystalline cellulose.

Keywords: *Heracleum Sosnovskyi* Extract; *Heracleum Sosnovskyi*; Furocoumarins; Xanthotoxin; Bergapten; Umbelliferon.

Creation of a Formulation of an Antibacterial Coating Based on Silver Nanoparticles for the Treatment of Office Surfaces

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21-23 February 2023

Poster: P152

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Abstract:

Creation of a formulation of an antibacterial coating based on silver nanoparticles for the treatment of office surfaces. The results of scientific research demonstrate a high risk of the spread of microbial and viral infections during the use of surface office equipment and stationery. The purpose of this work is to create a formulation of materials that can reduce the risk of infection in contact with office surfaces. The composition of the proposed coating includes silver nanoparticles, in quantities that allow for the suppression of pathogenic and conditionally pathogenic microflora. The coating is a varnish that ensures the application of a stable microfilm, which allows for wet cleaning, among other things.

Keywords: silver nanoparticles; microbiological contamination; biocidal coating.

Keywords: Silver Nanoparticles; Biocidal Coating; Microbiological Contamination.

Analysis of Some Indicators of the Quality of Jerusalem Artichoke Tubers (HELIANTHUS TUBEROSUS L.)

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21-23 February 2023

Poster: P153

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Abstract:

The increasing interest of researchers is the use of food plant materials containing a complex of biologically active substances that provide a versatile pharmacological effect. Such raw materials include Jerusalem artichoke tubers, traditionally used in the diet therapy of patients with diabetes mellitus, which is associated with a high content of inulin in raw materials. In order to standardize the Jerusalem artichoke raw materials, a chromatographic determination of the composition of monosaccharides, a quantitative assessment of the content of polysaccharide and pectin complexes of this raw material, inulin were carried out according to the methods traditionally used in pharmacopoeial analysis.

Keywords: Helianthus tuberosus; Inulin; Polysaccharide complex; Chromatographic analysis.

Metals Analysis in Convolvulus Pluricaulis Choisy Medicinal Plant Raw Materials

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Poster: P154

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Abstract:

Medicinal plants are able to accumulate both minerals and heavy metals from the environment. Proved that elements with biologically active substances provide the development of pharmacological effects, however, information about the elemental composition of individual species is very limited. Medicinal plant *Convolvulus pluricaulis Choisy* (Bindweed) is included in the Ayurvedic, Indian Pharmacopoeias and others. Shankhpushpi herb has nootropic, antioxidant, anticonvulsant and else pharmacological effects [1]. Medicinal plant raw materials are used in native powder form with a particle diameter of no more than 0.25 mm in tablets, capsules, as well as in syrup form to improve memory, cognitive functions, relieve anxiety and tension. The elemental composition study of *C. pluricaulis* herb powder was conducted to assess the possible minerals intake into the human body. Content analysis of Al, As, Ba, Bi, Ca, Cd, Co, Cr, Cs, Cu, Fe, K, Li, Mg, Mn, Na, Ni, Pb, Rb, Se, Sr, Zn was analyzed by atomic emission spectrometry. Sample preparation was realized by "wet" mineralization. The study results revealed Al, Ba, Ca, Cu, Fe, K, Li, Mg, Mn, Na, Rb, Sr and Zn in raw materials in range of 1.99-11120 mcg/g. Toxic elements Pb, Cd and As, as well as Bi, Ni, Cs, Se were also not detected. Discovered the metal content increased in a line (in mcg/g): Li (1.99)→ Cu (9.45)→ Rb (21.23)→ Zn (36.95)→ Ba (40.77)→ Sr (47.17)→ Mn (70.09)→ Fe (1317)→ Al (1432)→ Mg (2766)→ Na (3682)→ K (6299)→ Ca (11120). Ca, K, Mg, Na – macronutrients – amounted to 88.9%; toxic Al, Ba – 5.5%; essential Cu, Fe, Mn, Zn – 5.3%; potentially toxic Rb, Sr – 0.3%; conditionally essential Li – 0.01% of total elements content in medicinal raw materials. Determined the possible metals intake with Shankhpushpi powder is 0.001–133.4 mg per day with a double powder reception at 3-6 g dose.

Keywords: *Convolvulus Pluricaulis*; Shankhpushpi; Heavy Metals; Mineral Substance.

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Determination of Acrylamide in Biscuit Samples by New Microextraction Method and Gas Chromatography-Mass Spectrometry and Health Risk Assessment

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Abstract:

Acrylamide is a chemical compound that forms in the starch-containing food products during high-temperature cooking, including frying, baking, and roasting. This chemical pollutant can cause carcinogenesis, mutagenesis and reproductive toxicity in humans. Biscuit is a food product that is highly exposed to the formation of acrylamide and the desire to consume it is high in children and teenagers. The aim of this research was to develop and validate a new method for determining of acrylamide in biscuits using GC-MS, determine the amount of acrylamide in biscuit samples and evaluate the risk of carcinogenesis and non-carcinogenesis caused by its intake. Methods: In this research, a method for extracting and purifying of acrylamide using GC-MS was developed and validated. Then, the level of acrylamid was determined in 45 biscuit samples that were collected from the market in 2022. In addition, the non-carcinogenic risk (Target hazard quotient-THQ) and carcinogenic risk (incremental lifetime cancer risk-ILCR) and Margin of Exposure (MOE) of acrylamide intake through biscuit consumption were evaluated in children and adults. Results: The results showed that the mean concentration of acrylamide in biscuit samples was 1264.63 µg/kg. The calculated CDI for acrylamide in the tested biscuits showed that the intake of acrylamide in children was higher than in adults. The THQ in adults and children was in the safe range, with the difference that its level is lower in adults compared to children. The highest level of ILCR was observed in children (3-4 years old). The lowest level of ILCR was observed in men aged 25-64 years who consumed contaminated biscuits with acrylamide. For acrylamide, the lowest benchmark dose confidence limits for the 10% benchmark response (BMDL10) were 0.43 mg/kg bw/day and 0.17 mg/kg bw/day, derived respectively from experimental evidence of peripheral nerve axonal degeneration in male rats and harderian gland adenocarcinomas in mice The results of MOE (0.17) showed that the risk of carcinogenesis was high in all age groups due to exposure to acrylamide. Also, MOE (0.43) in age groups below 19 years showed that the risk of carcinogenesis due to exposure to acrylamide was high. Conclusion: The results showed that biscuit is one of the sources of acrylamide intake by Iranian people, and all consumers regardless of age may be at elevated carcinogenic risk.

Keywords: Acrylamide; Biscuit; Validation; Gas Chromatography; Mass Spectrometry; Risk Assessment.

Investigation of Natural 3-Phenyl Coumarin Analogues as Selective PLK1 Inhibitors for Treating Prostate Cancer Using Molecular Docking

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Poster: P156

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Abstract:

The Polo-like kinase 1 (PLK1) is a conserved subfamily of serine-threonine protein kinases that its forced expression was found to be carcinogenic. Therefore, PLK1 can be an attractive drug target for the treatment of tumor diseases such as prostate cancer. In this study, natural 3-phenyl coumarin analogues (glycycoumarin, licopyranocoumarin and isolicopyranocoumarin) were retrieved from PubChem server as 3D structures in SDF files. Crystal structure of PLK1 was obtained from Protein Data Bank (PDB) database (PDB ID: 2RKU). Then, the compounds with inhibitory potential were selected by molecular docking using Molecular Operation Environment (MOE) software, in terms of free energy binding against the PLK1. The results showed that compound licopyranocoumarin generated strongest binding affinity (-13.43 kcal/mol) against the target and bind significantly with some of the amino acid residues in the active site of PLK1 and thus could act as potential inhibitory compound against PLK1 protein.

Keywords: PLK1; 3-phenyl coumarin; Molecular docking.

Design and Synthesis of New 2-Mercaptoethanol Derivatives as Selective COX-II Inhibitors

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Poster: P157

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Abstract:

Non-steroidal anti-inflammatory drugs (NSAIDs) are used as antipyretics and analgesics, but due to gastrointestinal (GI) side effects, their use might be hampered in some patients. The main mechanism of action of NSAIDs is the inhibition of the cyclooxygenase (COX) enzymes. Cyclooxygenase converts arachidonic acid into prostaglandins (PGs) and thromboxanes. In recent years, two isoenzymes of cyclooxygenase have been discovered, COX-I and COX-II. COX-I is responsible for platelet aggregation, renal blood flow regulation, and synthesis of cytoprotective PGs in the Gastrointestinal tract, whereas COX-II is responsible for inflammatory processes and expressed in response to the release of endotoxins, mitogens, and cytokines [1, 2]. Also, COX-II is involved in the pathophysiology of many diseases, including various types of cancer and neurodegenerative diseases, such as Alzheimers and Parkinsons. Studies on selective COX-II inhibitors have shown that they are associated with a reduced risk of gastrointestinal complications compared to other NSAIDs [3]. Therefore, the aim of this study is to design and synthesize new 2-Mercaptoethanol derivatives as selective COX-II inhibitors. Materials and methods: The molecular modeling studies of 2-Mercaptoethanol derivatives were carried out using AutoDock software to search for suitable interactions between the ligands and enzyme. In order to synthesize chalcone intermediate, various derivatives of benzaldehyde and para-(methylsulfonyl)acetophenone react with each other in the methanol while utilizing NaOH as a catalyzer. Then, the chalcone derivatives react with 2-Mercaptoethanol in a chloroform medium. This step will be catalyzed by adding an appropriate amount of cinchonine. Finally, 2-Mercaptoethanol derivatives will be obtained after desire purification. Results: The docking studies demonstrated that the designed compounds would be capable to form strong hydrogen bond interactions between para-SO₂Me group and amino acids of the active site. The structures of these compounds were characterized by Mass, IR, and ¹H NMR spectra. Also, biological evaluation of the synthesized derivatives is in progress. Discussion: Based on performed docking studies, it was observed that para-SO₂Me pharmacophore of 2-Mercaptoethanol derivatives could insert into the secondary pocket present in COX-II isoenzyme and formed the proper interactions with Arg513 and His90, which is necessary for having selective enzyme inhibition. Conclusions: 2-Mercaptoethanol derivatives were designed based on the structure-activity relationship (SAR) of COX-II inhibitors. Thereafter, they were synthesized in a way so that obtained structures would match SAR results. Hence, it is expected that these compounds will have high potency and fewer side effects due to the selective inhibition of COX-II.

Keywords: COX- II; 2-Mercaptoethanol; synthesis; chalcone.

References:

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3. Giercksky, K.E., COX-2 inhibition and prevention of cancer. *Best Pract. Res., Clin. Gastroenterol.*, 2001. 15(5): p. 821-33.

Design, Molecular Modeling Studies and Synthesis of 4-Oxobenzothiazolopyrimidine -3-Carbohydrazide as Anti-HIV-1 Agents

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21-23 February 2023

Poster: P158

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Abstract:

Acquired immunodeficiency syndrome (AIDS) is a potentially life-threatening condition caused by two species of Lentiviruses, Human immunodeficiency virus (HIV) 1 and 2. HIV-1 is the most common cause of HIV/AIDS cases worldwide. As a retrovirus, HIV uses an integrase (IN) enzyme to catalyze the insertion of its viral DNA into the host DNA (specifically CD4+ T cells). As a result, IN can be a key target for inhibiting HIVs viral activity. Developing new anti-HIV treatments is ongoing research worldwide for many reasons, such as viral resistance and side effects of the current treatment protocol, "highly active antiretroviral therapy (HAART)." This study attempts to design and synthesize 4-oxobenzothiazolopyrimidine-3-carbohydrazide derivatives as novel IN inhibitors. Materials and methods: The catalytic core domain (CCD) of IN, which is considered the active site, consists of three acidic residues coordinating a bivalent metal ion. Considering the structure-activity relationships (SARs) of IN inhibitors and the pharmacophore needed for IN inhibitory activity, we designed and synthesized novel IN inhibitors. These compounds were prepared starting from the 2-aminobenzothiazole and ethoxy methylene malonic diethylester in 4 steps. The product of first step, diethyl 2-((benzo[d]thiazol-2-ylamino)methylene)malonate, yields ethyl 4-oxo-4H-benzo[4,5]thiazolo[3,2-a]pyrimidine-3-carboxylate by the ring closure reaction. Afterwards, by using hydrazine reagent, hydrazide intermediates are produced and reacts with isocyanate derivatives to give target compounds. Also, in this study, the potential affinity of each designed compound was evaluated prior to synthesis via molecular modeling tools such as docking, and the structure of each compound was validated after the purification of synthesized compounds. Results: The results from this study showed that the designed compounds are synthesizable, purifiable using crystallization techniques, and may have an inhibitory effect on IN. Also, molecular modeling results showed the main interactions of the hydrophobic pocket of CCD, and more importantly, charge transfer interactions of chelation motifs and Mg²⁺ ions. The interactions with Mg²⁺ and the docking score provided incentives for synthesis. Eventually, the structure of each synthesized compound was confirmed via spectroscopical approaches, including IR, LC-MS (ESI), and ¹HNMR. Discussion: The IN inhibitory activity of 4-oxobenzothiazolopyrimidine-3-carbohydrazide can be due to the chelating properties of this core structure. Mg²⁺ ions in the CCD of IN, which contribute to DNA incrtion, can be the first essential interaction to target in designing an anti-integrase. Other influential interactions are the hydrophobic interactions in the hydrophobic pocket of CCD. Conclusions: From this study, it can be concluded that the application of 4-oxobenzothiazolopyrimidine-3-carbohydrazide as the core of synthesis may result in considerable anti-IN activity. However, more studies are needed to investigate these compounds safety and efficacy in models closer to the condition of AIDS prior to clinical applications. Consequently, we anticipate more derivatives of 4-oxobenzothiazolopyrimidine-3-carbohydrazide in the paradigm of lead optimization to develop safer and more effective inhibitors.

Keywords: Human immunodeficiency virus; HIV integrase; The hydrophobic pocket of CCD.

References:

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Design, Synthesis, and Molecular Modeling of New Pyrimido [1,2a] Benzimidazole Analogues as anti-HIV agents

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21-23 February 2023

Poster: P159

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Abstract:

AIDS, or acquired immunodeficiency syndrome, is brought on by the HIV virus. Nearly 38 million individuals are AIDS sufferers as of right now. There are about 30 medications available to treat HIV infection that fall under these pharmacological categories: I. - Reverse transcriptase inhibitors II. - Protease inhibitors III. - Virus entry inhibitors (CCR5 antagonists and fusion inhibitors) IV. - Integrase inhibitors Due to its crucial function in the life cycle of the virus and the absence of a human comparable protein, the integrase enzyme has always been of interest as one of the therapeutic targets for the HIV-1 virus. The main focus of research has been on integrase enzyme inhibitors due to the toxicity and development of drug resistance to existing medications. Since there is no human homolog for these inhibitors, it is anticipated that they will have fewer adverse effects when used to treat HIV-1. A variety of inhibitor compounds were created in accordance with the pharmacophore of integrase inhibitors, which calls for the presence of a chelator and hydrophobic component, which is believed to inhibit this enzyme, hence halting the spread of HIV. Using a molecular modeling approach, novel compounds with chelator pharmacophoric groups are created with the intention of inhibiting the integrase enzyme. The compounds are synthesized, and their anti-HIV-1 properties are examined. Materials and methods: Utilizing molecular modeling and docking software, a new series of 1,3-diphenylpyrimidine-2,4,6-trione was synthesized. As 5-acetyl diphenylbarbituric acid and various benzaldehyde derivatives interacted in ethanol, the resultant intermediate and 2-aminobenzimidazole formed the target compound. Derivatives designed by the Hyperchem program and applying the MMX force field method were brought to the least energy to determine their best conformations. Electron pairs of amin chelate Mg of the integrase enzyme and deactivates it. Our target molecule was synthesized, and several analysis techniques including IR, ¹H NMR, ¹³C NMR, and mass validated this. The biological assay test will demonstrate the inhibitory impact that can compete with Raltegravir because of the excellent docking result and thoughtful design of the molecule.

Keywords: AIDS; HIV-1; Integrase inhibitors; diphenyl barbituric acid.

References:

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Design and Synthesis of New Aminoguanidine Derivatives as Selective COX-2 Inhibitors

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Abstract:

Cyclooxygenase (COX) enzyme is responsible for converting arachidonic acid to prostaglandins and thromboxanes. Non-steroidal anti-inflammatory drugs (NSAIDs) have been used over the last century to relieve pain and fever and play their pharmacological role by competitive inhibition of COX. There are two isomers of COX: COX-1 is involved mainly in renal and homeostatic procedures and establishes a protective layer in gastric mucous by producing PGs, whereas COX-2's primary role is in inflammatory processes and is produced in response to endotoxins and cytokines [1, 2]. Therefore, the extensive use of COX-2 inhibitors in inflammation, different kind of cancers, and some neurodegenerative diseases are entirely rational [3, 4]. Thus, this study was created to design and synthesize a new series of chalcone derivatives with the aminoguanidine group, which has the potential to inhibit the COX-2 enzyme selectively. Materials and methods: A new series of aminoguanidine derivatives was designed. Docking studies were performed using Autodock Vina software to predict the affinity of compounds and interactions with the enzyme. The synthesis process was carried out by reacting benzaldehyde derivatives and para-(methylsulfonyl) acetophenone in methanol with NaOH pellets. Then, the chalcone intermediates undergo the reaction with aminoguanidine in the presence of acid in THF for a 24 hours reflux or more [5]. Finally, the compounds were purified by recrystallization. Results & Discussion: Docking and molecular modeling studies indicated that the COX-2 selectivity effect is achieved by the SO₂Me group, which enters and interacts with the secondary pocket of the COX-2 enzyme, where oxygen atoms of the SO₂Me group form hydrogen bonds with Arg513, His90, and Phe518 in the side pocket of the COX-2 enzyme. A two-step reaction afforded the final products. After purification, the structures of these compounds were successfully characterized by Mass, IR, ¹H NMR, and ¹³C NMR spectra. Conclusions: According to the structure-activity relationship (SAR) of COX-2 inhibitors and previous studies, the new aminoguanidine derivatives were designed and synthesized as selective COX-2 inhibitors. Docking studies revealed the proper position of designed molecules in the COX-2 active site. IR, Mass, ¹H NMR, and ¹³C NMR spectra confirm the synthesis of the desired molecules. Biological assay tests will be measured, although considering the rational design of the structure and SAR studies high COX-2 inhibitory effect is expected.

Keywords: Aminoguanidine; selective COX-2 inhibitors; chalcone; cancer.

References:

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- Williams, C.S. and R.N. DuBois, Prostaglandin endoperoxide synthase: why two isoforms? *American Journal of Physiology*, 1996. 270(3 Pt 1): p. G393-400.
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- Jain, P., et al., Rational design, synthesis and in vitro evaluation of allylidene hydrazinecarboximidamide derivatives as BACE-1 inhibitors. *Bioorganic & Medicinal Chemistry Letters* 26 (2016) 33–37.

Design, Synthesis and Molecular Modeling Studies of New Diaryloxodihydropyrrole Derivatives as Selective Cyclooxygenase-2 Inhibitors

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Abstract:

Non-steroidal anti-inflammatory drugs are considered analgesic and anti-inflammatory, and their primary mechanism is the inhibition of cyclooxygenase enzyme. Cyclooxygenase is the key enzyme in the production of prostaglandin and thromboxane, and exists in three isoforms, called COX-1, COX-2, and COX-3. COX-1 is found in most normal cells and tissues and is responsible for the synthesis of prostanoids, which plays an important role in maintaining the normal physiology of the digestive mucosa, and kidney, and also regulating platelet activity. COX-2 enzyme is not normally present in the tissue, and is activated only during tissue damage and inflammation. Selective COX-2 inhibitors such as celecoxib and rofecoxib have fewer gastrointestinal side effects than aspirin, ibuprofen, and diclofenac, which inhibit both COX-1 and COX-2 enzymes. The recent market withdrawal of some coxibs due to their adverse cardiovascular side effects clearly delineates the need to develop alternative structures with COX-2 inhibitory activity. Therefore, in this study, new diaryloxodihydropyrrole derivatives were designed and synthesized based on the structure-activity relationship of selective COX-2 inhibitors, in order to introduce a novel scaffold with high selectivity and fewer side effects for COX-2 inhibition. Target compounds were synthesized in two steps. In the first step, 4-(methylthio)benzaldehyde, arylamine derivatives, and dimethyl acetylene dicarboxylate (DMAD) in the presence of para toluene sulfonic acid (PTSA) were stirred in ethanol for 48 hours. Then the resulting product was filtered off and recrystallized with ethanol. After that, a solution of Oxone and water was added to a well-stirred solution of the resulting product and diethylamine as a catalyst in acetonitrile. After the completion of the reaction, the resulting precipitates were filtered off and recrystallized with ethanol. A novel series of diaryloxodihydropyrrole derivatives was design and synthesized as selective COX-2 inhibitors in good yields. Molecular modeling studies revealed that the compounds were well placed in the active site of COX-2 enzyme. The structure of synthesized compounds was confirmed by different analysis methods including FT- IR, ¹H-NMR, and MASS spectroscopies. The COX-2 inhibitory activity of these compounds is under investigation.

Keywords: Diaryloxodihydropyrrole; Synthesis; Design; Selective COX-2 inhibitor.

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Design, Synthesis and Docking Studies of New 1-Alkyl-2-Aryl-Pyrrolin-5-one Derivatives as Selective Cyclooxygenase-2 Inhibitors

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21-23 February 2023

Poster: P162

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Abstract:

Nonsteroidal anti-inflammatory drugs (NSAIDs) can reduce inflammation, pain, and fever. They inhibit an enzyme called cyclooxygenase. This enzyme produces substances called prostaglandins, that cause inflammation and pain in the body. There are two types of cyclooxygenase enzymes. COX-1 which has physiological roles in the body is expressed in many tissues and shows important effects in homeostasis maintenance. COX-2 is the inducible isozyme and has roles in pathological conditions such as inflammation. NSAIDs reduce pain, fever and inflammation by inhibition of both COX-1 and COX-2. COX-1 inhibitory activity of NSAIDs leads to some side effects like renal dysfunction and gastrointestinal ulcers. Accordingly, it was expected that selective inhibition of COX-2 could reduce gastrointestinal side effects of NSAIDs while exhibiting desirable anti-inflammation effects of them. Therefore, many different selective COX-2 inhibitors have been synthesized and evaluated to have less gastrointestinal side effects than NSAIDs. New drugs of this family, such as celecoxib and rofecoxib, are COX-2 specific inhibitors, and therefore have fewer gastrointestinal side effects. Increased risk of cardiovascular event in some selective COX-2 inhibitors such as rofecoxib, led to voluntarily withdrawing of this drug from the market. As a result, in this research, new 1-alkyl-2-aryl-pyrrolin-5-one derivatives were designed and synthesized based on the relationship structure-activity of selective COX-2 inhibitors. Target compounds were synthesized in two steps. In the first step, 4-(methylthio)benzaldehyde, alkylamine and allylamine derivatives, and dimethylacetylenedicarboxylate (DMAD) in the presence of para toluene sulfonic acid (PTSA) were stirred in ethanol for 72 hours. After the completion of the reaction, the resulting product was filtered off and recrystallized with ethanol. In the second step, a solution of Oxone and water was added to a well-stirred solution of the resulting product and diethylamine in acetonitrile. After the completion of the reaction, the resulting precipitates were filtered off and recrystallized with ethanol. In this study we designed and synthesized some new 1-alkyl-2-aryl-pyrrolin-5-one derivatives as selective COX-2 inhibitors. Docking studies of these compounds showed that they were well placed in the active site of COX-2 enzyme. The structure of synthesized compounds was confirmed by FT- IR, ¹HNMR, and MASS spectroscopies. The COX-2 inhibitory activity of these compounds is under investigation.

Keywords: Pyrrolin-5-one; Synthesis; Design; Selective COX-2 inhibitors; Docking studies.

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Antidepressant Activity of New Derivatives of Thietanyltriazolone and 5-Aminoaminopyrazole

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21-23 February 2023

Poster: P163

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Abstract:

Previous studies revealed significant psychotropic activity thietanyltriazolone derivatives (TTD) and 5-aminoaminopyrazole derivatives (5-AAP) (1). Materials and Methods The antidepressant activity of 3 new TTD (GR46; GR43; GR78) and 5-AAP (SHS67/1) was studied in male mice (n=42) in the forced-swim test (FST) and the tail-suspension test (TST) (2,3). TTD and 5-AAP were injected once intraperitoneally (i.p.) at doses 10,2 mg/kg; 8,4 mg/kg; 9,7 mg/kg; 12,3 mg/kg respectively compared to the control group. The reference drug amitriptyline was injected i.p. once at a dose of 10 mg/kg. The immobility time (IT) was evaluated in TST; the IT and index of depression (ID) were assessed in FST. Results All the TTD and 5-AAP caused antidepressant-like effect in FST similar to amitriptyline: they significantly reduced ID by 27.1-66.7% compared to the control group. TTD didn't change IT in TST, while 5-AAP significantly reduced it by 51.8% compared with the control group. Discussion and conclusion All the molecules showed antidepressant-like activity similar to amitriptyline, which makes them perspective for the further studies.

Keywords: Antidepressant Effect; Thietanyltriazolone; 5-Aminoaminopyrazole; Tail Suspension Test; Forced Swimming Test

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TLC-Screening of Antihypertensive Pharmaceutical Drugs

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21-23 February 2023

Poster: P164

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Abstract:

Calcium channel blockers have been important in clinical practice for a long time due to the spread of cardiovascular diseases on a global scale. Based on this, it is necessary to develop screening methods for differentiating antihypertensive drugs in the biomaterial and their subsequent chemical-toxicological analysis. Objective: to determine the optimal conditions for screening antihypertensive drugs by thin layer chromatography. Materials and Methods: The objects of study were amlodipine standard sample (Anhui Minmetals Development I/E LTD, China), Koronim tablets (Nobel Almaty Pharmaceutical Factory JSC, Kazakhstan), Verapamil tablets (AVVA RUS JSC, Russia), Nifedipine tablets (PJSC Tekhnolog, Ukraine), Diltiazem tablets (G.L. PHARMA, GmbH, Austria). A set of instruments for TLC: chromatographic plates "Sorbfil PTSH-AF-V-UF" 10x10 cm, microsyringes "MSH-10", "MSH-1" (Tsvet); chromatographic chambers, UV chromatoscope (Lenchrom, UV cartridges 254/365); reagents and solvents of the category "chemically pure" and "analytically pure": chloroform, hexane, acetone, ethyl acetate, butanol, ethanol 90%. Results and discussion: Isolation of drug mixtures from biological material was carried out by liquid-liquid extraction. The selection of a solvent system for the detection of toxicants by TLC screening was carried out in accordance with the recommendations of the Stahl series and the International Association of Toxicologists. During the experiment, butanol, acetone, chloroform, diethyl ether, chloroform, 25% ammonium hydroxide, etc. were used. Studies have shown that in the mobile phase, consisting of a mixture of diethyl ether, acetone and butyl alcohol in a ratio of 10:5:5, the mobility of the studied substances is not high enough, analytical spots remained on the start line. In the mobile phase, consisting of chloroform-acetone (1:1), the mobility of toxicants was high, the spots were close to the finish line. In addition, it was found that extraneous spots appeared in the staining zone of the test solution, which indicates that the cleaning process was insufficient. In the diethyl ether-acetone-ammonium hydroxide (20:20:1) system, verapamil was well distributed, and amlodipine was located close to the start line. Nifedipine and diltiazem did not rise above the start line. In the butanol-acetone (5:5) system, selective separation of amlodipine, nifedipine, diltiazem, and verapamil is observed, with the R_f values being for nifedipine - 0,40±0,03, verapamil - 0,68±0,03, diltiazem - 0,58±0,03 and amlodipine - 0,31±0,03. The following reagents were used as detectors: UV light, reagents of Dragendorff, Mandelin, Lieberman, Frede, Markey, conc. sulfuric acid, conc. nitric acid, 5% iron (III) chloride solution. The sensitivity of the reagents ranged from 0.5 to 10 µg. UV light turned out to be the most sensitive of the detectors; therefore, the method was chosen as optimal. Conclusion: Thus, the selective separation of antihypertensive drugs isolated from biological material by TLC was observed using the mobile phase of butanol - acetone (5:5), with a UV detector at a wavelength of 254 nm.

Keywords: Thin-Layer Chromatography; Screening; Amlodipine

References:

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Spectral Characteristics of a New Biologically Active Derivative of Xanthine

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21-23 February 2023

Poster: p165

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Abstract:

The spectral characteristics of a new biologically active derivative of xanthine – 1,3-dimethyl-7-thietane-8-dimethylaminoethylaminoxanthine have been studied. The IR spectra of the compounds were taken on a spectrometer in disks with potassium bromide in the range from 4000 to 400 cm⁻¹. IR spectroscopy data showed the presence of the following characteristic absorption bands: in the region of 1042 cm⁻¹, valence vibrations of the thiogroup (-S-) are observed, and the absorption bands in the region of 1548 cm⁻¹ correspond to valence vibrations of carbon-nitrogen bonds (C=N), in the region of 1651, 1677 cm⁻¹ carbonyl group (C=O). Characteristic absorption bands of valence vibrations of carbon-carbon and carbon-nitrogen bonds of the purine ring are observed at 1503, 1417, 1337 cm⁻¹. The NMR spectroscopy data were studied under conditions of ¹H and ¹³C NMR chemical shifts: the corresponding frequency representations were recorded in the spectra of the substance under study and deciphered from the literature data. The NMR spectrum showed resonances for the thietane ring and methylxanthine, dimethylaminoethylamine substituent in the form of a doublet at 4.8, 8.5 and 82.5 ppm. The study of samples by gas chromatographic mass spectrometry showed the presence of the following parameters: in chromatograms, each peak corresponded to a specific cation formed during ionization and as a result, the molecular weight was 338.1 m/z. The spectral characteristics of the samples under study will be incorporated into the draft regulatory document for the identification of the substance.

Keywords: Xanthine; IR-Spectroscopy; NMR-Spectroscopy; GC-MS; Identification

Design and Synthesis of Tetrahydroquinoline Analogs as Selective COX-2 Inhibitors

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21-23 February 2023

Poster: p166

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Abstract:

Non-steroidal anti-inflammatory drugs (NSAIDs) have been widely used for almost a century due to their relieving fever and pain effects, but due to unwanted gastrointestinal system side effects, the tolerance of these drugs is limited by patients. The therapeutic effects of these drugs are caused by inhibiting the enzyme cyclooxygenase (COX). Two cyclooxygenase isozymes have been discovered: COX-I function is responsible for renal and hemostatic effects, while COX-II is responsible for inflammatory processes [1,2]. Therefore, the widespread and common use of COX-2 selective inhibitors in the treatment of pain and inflammation, as well as the proof of the pathological role of this enzyme in many diseases such as cancers and neurodegenerative diseases such as Alzheimers and Parkinsons, has led to greater acceptance, to find more effective COX-2 enzyme inhibitor drugs [3]. Therefore, in this study, a series of new 2,4-diphenyltetrahydroquinoline with the potential of selectively inhibiting the COX-2 enzyme and a more suitable safety profile has been designed and synthesized based on the structure-activity relationship of these inhibitors. According to the COX-2 inhibitors structure-activity relationship (SAR) and literature review of these compounds, a new series of tetrahydroquinoline derivatives containing SO₂Me pharmacophore at the para position of one of the phenyl rings were designed. The docking studies of designed compounds into the COX-2 active site were performed by Autodock Vina software. For the synthesis of these compounds, first, different derivatives of chalcone were synthesized from the reaction of various derivatives of benzaldehyde with para-(methylsulfonyl)acetophenone (as a starting material) in the presence of NaOH pellets in methanol solvent. Finally, these chalcone derivatives were reacted with ammonium acetate, cyclohexanone, pyrrolidine, and iodine under an oxygen atmosphere. As a result, various derivatives of tetrahydroquinoline, which were purified by plate chromatography, were obtained [4]. The docking studies indicated the hydrogen bonding between the oxygen atom of SO₂Me pharmacophore with the NH group of His90 and Arg513 in the secondary pocket of COX-2 enzyme. The synthesized compounds were purified, and the structures were characterized by Mass, IR, and NMR spectra. Discussion: Docking and molecular modeling studies demonstrated desirable interactions between crucial amino acids in the COX-2 active site and designed ligands. All compounds are successfully synthesized via two-step reactions and characterized by different spectra. Based on the structure-activity relationship of COX-2 inhibitors and molecular modeling studies, the designed tetrahydroquinoline derivatives are expected to have a suitable inhibitory effect on the enzyme and fewer adverse effects.

Keywords: Synthesis; COX-2; Tetrahydroquinoline; Chalcone

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Study of Restoring Properties of Rutin and Troxerutin in Solutions and Gels

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21-23 February 2023

Poster: P167

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Abstract:

form of a solution and gel) have been chosen as antioxidant substances. Observations of the reducing properties have been carried out with the use of model mediator system $K_3[Fe(CN)_6]/K_4[Fe(CN)_6]$, where Fe(III) was an oxidant reagent. Reducing properties were characterized according to the changing red/ox potential of the studied system during the storage period. The studied samples were stored in a thermostat in accelerated aging mode. Results: there was a decrease of red/ox potential during the experiment that indicates restoring activity of the studied substances. It also has been demonstrated that restoring properties of rutin and troxerutin in aqueous solutions and gels are maintained throughout the experiment.

Keywords: Restoring Activity; Potentiometry; Rutin; Troxerutin

Development of Intranasal Delivery System Based on Ion-Sensitive in Situ Matrices

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21-23 February 2023

Poster: P168

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Abstract:

One of the promising areas in pharmaceutical technology is the development of intranasal drug delivery systems. To prevent the effect of mucociliary clearance on the drug it is possible to use in situ matrices in order to increase the exposure time of the dosage form on the surface of the mucous membrane of the nasal cavity. The most suitable matrices are ion-selective polymers that perform rapid sol-gel transition in contact with the mucous membrane of the nasal cavity. Gellan gum-based matrices suitable for nasal delivery of both immunobiological and synthetic substances have been developed and tested.

Keywords: In Situ Systems; Intranasal Administration; In Situ Polymers; Gellan Gum

In Recent Years, Rosacea Has Become Very Widespread. a Treatment Option for This Disease is The Use of a Cream with Photoprotective Properties

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Poster: p169

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Abstract:

1) Rosacea or acne rosacea is a chronic, recurrent skin disease that most often affects the skin of the face. 2) The main ingredients of the cream: succinic acid, zinc oxide, titanium dioxide. Excipients: hydroxyethyl cellulose, purified water, lutrol, cremophore. 3) In the course of experimental studies, the most optimal composition of the cream was selected. 4) The developed cream meets all the requirements for quality indicators.

Keywords: Rosacea; Succinic Acid; Cream

Development of The Composition and Technology of Suppositories for Relieving Muscle Spasm

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21-23 February 2023

Poster: P170

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Abstract:

Muscle spasm is a persistent inadequate tension of a muscle or its separate section. In some cases, herbal preparations may be effective for muscle spasm. In particular, it is known that in folk medicine, marsh saber (*Comarum palustre* L.) is used to treat these diseases. The purpose of the work is to develop the composition and technology of suppositories to relieve muscle spasm. To achieve this goal, it is necessary to solve the following tasks: 1. To develop the composition of suppositories based on the extract of marsh saber; 2. To develop a technological scheme of suppositories with marsh saber extract to relieve muscle spasm 3. To investigate the physical, physico-chemical and technological properties of suppositories based on the extract of marsh saber. Suppositories are the most convenient and simple dosage form to use in the treatment of various diseases. In addition, the use of medicinal substances in the form of suppositories makes it possible to achieve a faster therapeutic effect, with minimal losses of active substances. Because medicinal substances injected through the rectum are rapidly absorbed into the general bloodstream, bypassing the gastrointestinal tract and liver, where substances are partially destroyed.

Keywords: suppositories; pharmaceutical technology; herbal preparations; muscle spasm

Development of Technology and Composition of Foams with Nifedipin

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21-23 February 2023

Poster: P171

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The aim of our study is to theoretically substantiate and experimentally develop the formulation and technology for manufacturing foam with nifedipine, which contains its solid dispersions. The active pharmaceutical substance is nifedipine, which is a slightly water-soluble substance, which has a negative effect on the degree of release of the substance from the delivery system. This entails a decrease in pharmaceutical availability, and then pharmacological activity. The increase in pharmaceutical availability in the future can be used to reduce dosage and predict a decrease in side effects on a living organism. Four samples of foams were made and then studied, two of which were presented without a solid dispersion of nifedipine. The results show the effect of the polymer on the solubility of nifedipine in the "Foam" dosage form in comparison with the industrial analogue, which is presented in the form of a gel.

Keywords: Nifedipine; Foam; Disperse

Increasing The Solubility of the Anthelmintic Preparation by The Method of Solid Dispersions

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21-23 February 2023

Poster: P172

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Abstract:

The effect of obtaining solid dispersions with polyvinylpyrrolidone-24000 (PVP) on the solubility of albendazole in water was studied. Albendazole is an anthelmintic. The low solubility of albendazole in water limits its use, causing difficulties in the technological plan and significantly reduces bioavailability. The "solid dispersion method" significantly increases both the solubility and the release of a number of active substances from various dosage forms. Solid dispersion is a poly component system consisting, as a rule, of one or more active substances and (polymer) carrier matrix. Includes the phase of the dispersed substance and its solid solutions. Sometimes it is possible to form any complexes of various compositions with carrier polymer molecules. Materials and methods. The substance of albendazole was investigated. In the role of a carrier polymer, PVP-24000 was used to obtain dispersions. Medium-molecular fractions of PVP are plasma substitutes (in the form of injectable solutions). High – molecular fractions are prolongators of other dosage forms. Based on the PVP class, a number of auxiliary products have been developed that are used exclusively in pharmaceutical technology. the dispersions in the work were prepared by the method of "total solvent removal". Results. The production of solid dispersions increases both the solubility and the dissolution rate of albendazole. The solubility of albendazole from solid dispersion increases by 132-181 times compared to its initial substance. A set of methods of physical and chemical analysis, including: spectrophotometry in the UV region, microcrystalloscopy, the study of the optical properties of the studied solutions, allows us to assert: the increase in the solubility of albendazole from the obtained solid dispersions is due to the loss of crystallinity of the substance, the formation of a "solid solution" of albendazole in PVP, the solubilizing effect of PVP, as well as the production of a colloidal solution of albendazole during subsequent dissolution in water of solid dispersion. Conclusion. The formation of solid dispersions with PVP improves the dissolution of albendazole in water. The results obtained in the work are planned to be actively used in the further development of fast-soluble (effervescent) dosage forms of albendazole with increased bioavailability and accelerated release. Keywords: albendazole, solubility, solid dispersion, polyvinylpyrrolidone

Keywords: Albendazole; solubility; solid dispersion; polyvinylpyrrolidone

Technology for Obtaining Pellets with Isoniazide and Ofloxacin, Research Results

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21-23 February 2023

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Abstract:

Today, tuberculosis affects about 1/3 of the worlds population. Pulmonary tuberculosis is an infectious disease that ranks second among infectious diseases in terms of mortality. The main anti-tuberculosis drug is isoniazid, which has a number of adverse reactions on the body, including hepatotoxicity. Examining the register of medicines, it turned out that the combination drug containing isoniazid and ofloxacin is not yet available. To create such a drug, it is necessary to solve many problems, including the substantiation of the composition of excipients, which will optimize the release rate of active substances and ensure a therapeutic concentration in the blood serum for a sufficiently long time on the one hand and reduce toxic properties on the other hand. Development of the composition and technology for obtaining drugs in the form of dragees with isoniazid and ofloxacin. Dragees are intended for treatment at the site of localization, as they contain the active ingredient ofloxacin, a broad-spectrum antibiotic that acts on the DNA-gyrase of a bacterial cell, causing a bactericidal effect, isoniazid, which has anti-tuberculosis, antibacterial and bactericidal effects. The results of studying the dynamics of the process of releasing the active substances of isoniazid and ofloxacin in vitro on the degree of dispersion of the studied substances led to the conclusion that grinding in dry form, as well as when choosing an auxiliary liquid for dispersion, leads to a slight increase in release, ethanol is shown to be the best auxiliary liquid, with the release of isoniazid up to 91% and ofloxacin up to 99%. release of isoniazid and ofloxacin in an alkaline environment. Within an hour, more than 95% of the analytes are observed in the dialysis environment. The high release of isoniazid from the dosage form is due to its good solubility in water. The high level of release of ofloxacin is due to the introduction of povidone, so ofloxacin is released by 60 minutes by 95%. (HPLC). Dragees containing a therapeutic complex, including isoniazid 300 mg and ofloxacin 400 mg, are intended for the treatment of tuberculosis, have a mechanism for releasing isoniazid and ofloxacin, dragees are recommended to be used once a day. The agent dissolves within an hour after ingestion. It is known that isoniazid and ofloxacin have a hepatotoxic side effect, so we suggest taking this dosage form together with antioxidants. To confirm our hypothesis, studies were carried out in the presence of the polyphenolic flavonoid rutin. Animals received an oral dosage form with isoniazid and ofloxacin together with rutin at a dose of 50 mg/kg. There is a significant decrease in LPO (lipid peroxidation) with the introduction of the drug in combination with rutin. We consider it expedient to prescribe this combination in combination with natural or synthetic antioxidants. Conclusion. Thus, the composition and technology for obtaining dragees with isoniazid and ofloxacin have been developed. Studies have been carried out to study the release kinetics and standardization of the developed drug. Based on the obtained data, we came to the conclusion that the combination of isoniazid with ofloxacin will be the most effective and economical. In pharmacokinetic studies, a longer period of elimination of ofloxacin has been established, which together allows, when taken orally, to achieve an effect in patients with moderate and severe respiratory infections.

Keywords: Dragee; ofloxacin; Tuberculosis; isoniazid

The Activity of Silver Nanoparticles Synthesized from Various Extracts of Peganum Harmala on Microorganisms

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21-23 February 2023

Poster: P174

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Abstract:

The use of nanoparticles in medicine is growing more and more every day. Our research studied an aqueous extract of the plant Peganum Harmala. We synthesized silver nanoparticles in the obtained extracts and proved their presence by UV-spectroscopy. Extracts containing silver nanoparticles were tested on various microorganisms and showed a relatively increased fungistatic effect, unlike extracts that do not contain silver nanoparticles. The use of nanoparticles in medicine is growing more and more every day. Various physical and chemical pathways were used to synthesize nanoparticles. The chemical method of nanoparticle synthesis is extremely costly with additional environmental and biological risks. At the same time green synthesis pathways are simple, safe, non-toxic and environmentally friendly methods for the synthesis of nanoparticles of various metals by using bioactive compounds of plants, algae, fungi, yeast etc. Silver nanoparticles (Ag) are considered as the most economical and best alternative method among all available methods. Objective: To synthesize silver nanoparticles from extracts of Peganum harmala and to determine their effect on microorganisms. Methods: We have studied the water extracts of the leaves and seeds of Peganum harmala. Extracts of harmala seeds and leaves were obtained as follows. Dried seeds and leaves were grounded into powder and extracted by maceration. Then the mixture was filtered from the solid residue, the filtrate was centrifuged at 6000 rpm for 45 minutes, separated from the residue by decantation, and stored in a dark bottle in the refrigerator for further experiments. Argentum nitrate (0.001M) was used for the synthesis of silver nanoparticles in extracts of seeds and leaves of harmala. Research results: Mixtures of extracts of harmala seeds and leaves were mixed with a solution of silver nitrate in a ratio of 2:98. The mixtures were incubated for a day. On UV spectra's, it can be seen that silver nanoparticles are formed both in seed extracts and in leaves, which have a wide absorption band in the region of 430-450 nm. The mixtures were tested and showed pronounced fungistatic activity. Conclusion: Thus, we synthesized silver nanoparticles in water solutions of medicinal plant from the leaves and seeds of Peganum harmala. The conducted tests of extracts with silver nanoparticles on various microorganisms showed positive results compared to the original extracts. This indicates that the biological activity of extracts from Peganum harmala seeds and leaves is enhanced by the presence of silver nanoparticles.

Keywords: silver nanoparticles; water extracts of plants; fungistatic activity; Peganum harmala.; Fusarium sp.; Colletotrichum sp.

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Predicting Milk/Plasma Ratio (M/P) of Chemicals in Human Breast Milk with their Structural Characteristics

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21-23 February 2023

Poster: P175

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Abstract:

Feeding infants with safe milk from the beginning of their life is an important issue. Consuming permeable drugs during breastfeeding period by mother, could lead to serious side effects to the infant. To obtain the milk to plasma (M/P) concentration ratio, analytical methods such as high-performance liquid chromatography (HPLC) have been used [1]. However, many factors including laboratory condition and lactation time can affect the M/P ratio [2]. The aim of this study is to develop mechanistic models to predict the M/P ratio of drugs during breastfeeding period based on their structural descriptors. Methods: Two hundred and nine different chemicals with their M/P ratio were used in this study. They were categorized into two groups based on their M/P value: 1: Drugs with $M/P > 1$, considered as high risk 2: Drugs with $M/P < 1$, considered as low risk Thirty-eight chemical descriptors were calculated by ACD/labs and Data warrior software to assess the penetration of drugs during breastfeeding period. Later on, four specific models based on the number of hydrogen bond acceptors, polar surface area, total surface area and number of acidic oxygens were established for the prediction. The mentioned descriptors can predict the penetration with an acceptable accuracy. For the remaining compounds of each model, binary regression with SPSS 21 was done in order to give us a mechanistic model. Only structural descriptors with p-value

Keywords: Milk; Prediction; Descriptors

Antimicrobial and Antifungal Activity of Cell-Free Medium of *Spirulina platensis* Culture and Its Polysaccharide Extract

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21-23 February 2023

Poster: P176

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Abstract:

Cyanobacteria are the photosynthetic prokaryotes with a wide range of active metabolites. Among them, *Spirulina platensis* (*Arthrospira platensis*) is a microscopic and filamentous cyanobacterium that contains up to 60%–70% protein, 6%–12% polysaccharide, and a variety of vitamins, fatty acids, and minerals. Moreover, *Spirulina* exhibits a number of biological activities and can play valuable roles in the fields of medicine and healthcare. Water-soluble Polysaccharides of *Spirulina platensis* (PSP) have been approved for their antitumor, antioxidant, antimicrobial, antifungal, and antiviral activities. Method and Results: In this study, *Spirulina platensis* was cultured in Zarouk medium and after 25 days, the biomass was separated from culture medium. The biomass free culture medium, named as cell-free culture medium, was divided in two parts, one part was dialyzed using dialysis tube with cutoff 14KDa (named as sample D), and another part was precipitated with 5 volume absolute ethanol, then, precipitated part was dissolved and digested with pepsin to remove protein fraction. Again, precipitated with absolute ethanol. Precipitated polysaccharides were dissolved in distilled water (named as sample R). The polysaccharide extraction of biomass was also performed using hot water extraction in alkaline condition followed by similar methods as described for cell-free culture medium (named as sample T). Residual protein and carbohydrate content of each sample were assessed by Bradford and phenol sulfuric acid methods, respectively. The antibacterial and antifungal activity were evaluated using agar well diffusion method. Results: The protein content of sample D was calculated around 9 µg/mL, while the carbohydrate content was around 4.5 mg/mL. The protein content of R and T samples were less than 0.001 and around 0.2 µg/mL, respectively. The carbohydrate content of R and T samples were 55 and 31 µg/mL, respectively. All samples exhibited antifungal activity against *Candida albicans* and *Aspergillus niger*. They also have antibacterial activity against both Gram-positive and Gram-negative bacteria including *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Enterococcus hirae*, and methicillin-resistant *S. aureus*. As the antibacterial and antifungal activities of R is significant regarding the lesser content of carbohydrate and near the absence of protein content, it seems the most active antimicrobial component of sample D might be the polysaccharide content. Conclusion: Although more structural and functional studies are needed to find potent therapeutic candidates, the finding of this study showed that more than the biomass extract, the excreted bio macromolecules of *Spirulina platensis* in the culture medium can be considered as potent antimicrobial agents.

Keywords: Cyanobacteria; *Spirulina platensis*; Antimicrobial; antifungal; polysaccharide

Evaluation Aggregation Function of Thrombocytes in Vitro - A Universal Screening Model for Potential Drug- Candidates

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21-23 February 2023

Poster: P177

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Abstract:

Today, diseases of the cardiovascular system are critical to any healthcare system. In this regard, the issue of developing new, more effective and safe drugs is becoming more acute. Optical aggregation is a low-cost, technically simple and fast method for assessing platelet hemostasis and the properties of drug candidates at the preclinical stage. This method allows in vitro evaluation of the anti- and decontamination properties of platelets. The effectiveness of the method is proved by conducting an experiment with pentoxifylline. So pentoxifylline reduces platelet aggregation by 17,9% compared with the control measurement. Thus, the assessment of platelet aggregation ability can be used as a method for evaluating potential drugs.

Keywords: Platelets; Hemostasis; Agregtion

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Thalidomide's Infamous Past and What We Can Learn from It

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21-23 February 2023

Poster: P178

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Abstract:

Thalidomide was first developed in the USA in the early 1950s. It was marketed as a sedative that might be used to treat morning sickness in pregnant women. However, this medicine was later found to possess teratogenic properties that induce a range of birth defects. The studies of the mechanisms of action of thalidomide have led to the conclusion that it binds to the receptor named cereblon which further degrades the substrates, IKZF1 and IKZF3, that are essential for the proliferation of myeloma cells. Therefore, it has a teratogenic effect on the fetus. The metabolism of thalidomide involves non-enzymatic hydrolysis which leads to its further elimination with the urine in the form of hydrolytic metabolites and the leftover amounts detected is negligible. For the first time, in 1961, when two physicians who were working with this medicine, they had noticed an occurrence of serious birth defects in children born to women who had taken the drug. One in every five infants had the probability of acquiring the deformity. Phocomelia was reported to be the commonest deformity in which the limbs are extremely shortened or even completely absent sometimes, the condition being called amelia. The malformation of the thumb, intestines and heart defects were also observed. The studies in animals have confirmed the presence of similar teratogenic effects: mice fetuses whose mothers were fed thalidomide daily developed only one kind of anomaly called fetal resorption, or the partial or complete dissolution of fetal tissues after some embryos had died in uterus. This experience has helped us to come to the conclusion about the importance of observing the effects of the drugs consumed by pregnant women. Also it helped us to understand the importance of the performance of the toxicological analyses that would help us to avoid the dramatic consequences of the intake of various drugs.

Keywords: Teratogenicity; Thalidomide; Phocomelia; Amelia; Deformities; Birth defects

Thrombosis of The Inferior Vena Cava - a Universal Model for Screening Potential Drug - Candidates

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21-23 February 2023

Poster: P179

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Abstract:

Venous thrombosis is a syndrome characterized by blockage of one or more superficial or deep veins by a blood clot (thrombus) and a number of pathophysiological reactions (including pain, swelling, trophic disorders), the severity of which is directly dependent on the size and location of the thrombus, degree shunt, compensatory capabilities of the body and the severity of background diseases. And its catastrophic complication - pulmonary embolism (PE) - remains the most urgent disease. The problem of their occurrence, prevention and treatment has not been resolved and is debatable in many aspects. In recent years, the steady increase in thrombotic vein lesions is associated with common hereditary and acquired disorders in the blood coagulation and anticoagulation systems, the lack of control over the use of hormonal drugs, the high prevalence of oncological diseases, diseases that cause damage to the blood coagulation system, such as COVID-19 and traumatic lesions venous highways, as well as the general aging of the population. Therefore, the search for drugs to reduce the risk of thrombotic lesions, as well as to mitigate the consequences of an already occurring thromboembolus, is more relevant than ever. Thus, our model makes it possible to simplify and secure for a person the search for drug candidates for the treatment and prevention of thromboembolic lesions.

Keywords: Thrombosis; inferior; vena; Screening; Potential; Drug

The Protective Effect of Healthy Mitochondria Administration in Cadmium and Lead-Induced Toxicity on Rat Renal Proximal Tubular Cells

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21-23 February 2023

Poster: P180

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Abstract:

Lead (Pb) and cadmium (Cd) are known as toxic agents that are considered in different diseases etiology and contribute to mitochondrial functions disruption. Mitochondrial administration therapy could be applied with the purpose of replacing dysfunctional mitochondria with healthy ones and consequently, solving the mitochondria-related diseases. In the past decade, both in vivo and in vitro investigations were carried out on the immune-protective potential of isolated mitochondria. The mitochondria administration effects on the Pb/Cd-induced cytotoxicity of renal tubular proximal (RPT) cells were evaluated in current study. Findings indicated that Pb (10 μ M) and Cd (30 μ M)-induced toxicity on RPT cells, which included reactive oxygen species (ROS) generation, induction of lipid peroxidation (LPO), lysosomal membrane damage, mitochondrial membrane potential (MMP) collapse; moreover, the reduced glutathione (GSH) content was decreased. It was also found that the mentioned cells showed the increase of oxidized glutathione (GSSG) and changes in adenosine triphosphate (ATP). Results showed that RPT cells protection against Pb/Cd-induced cytotoxicity could be achieved through adding fresh mitochondria from liver, kidney and heart. Moreover, the mitochondrial internalization into RPT cells is mediated by actin-dependent endocytosis. Therefore, it could be proposed that the treatment of Pb/Cd-induced cytotoxicity could be carried out through mitochondria administration

Keywords: Mitotherapy; Cadmium; Lead

Design And Synthesis of Novel Derivatives of Phenylcarbamothiol Hydrazineyl Acetamide With The Probable Potential of *H. Pylori* Urease Inhibition Activity

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21-23 February 2023

Poster: P181

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Abstract:

Since drug resistance of *H. pylori* against antibiotics is rising sharply, therefore the design of new agents with various therapeutic mechanisms in this area is an attractive target for medicinal chemist. In addition, urease has been discovered as the key virulence factor of many microorganisms such as (*H. pylori*). Urease (EC 3.5.1.5) is the main enzyme for the hydrolysis of urea into ammonia, and given that this process is an essential pathway for the energy supply of bacteria, so, inhibition of urease can be useful for the elimination of bacteria. Therefore, the project effort is to design and synthesized new compounds based on inhibition of urease activity. Through the synthesis method is based on hybridization strategy through introduction of the new scaffold consist of; phenylisothiocyanate, hydrazine, phenoxy acetamide derivatives will be prepared.

The title compounds were obtained via a 4-step synthesis. In the first step, 2-chloro-N-phenylacetamide (compounds 3a-g) were obtained through the reaction of various aniline derivatives with chloroacetyl chloride under suitable reaction conditions. In the second step, 2-(4-formyl-2-methoxyphenoxy) N-phenylacetamide derivatives (compounds 5a-g) were created through the reaction of vanillin with (compounds 3a-g). In the third step, N-phenylhydrazine carbutamide (compound 8) was obtained through the reaction of phenylisothiocyanate and hydrazine hydrate. In the last step, the target derivatives (compound 9a-g) were synthesized through the interaction of compound 5a-g and (compound 8) under appropriate conditions. After the completion of the reaction, the resulting precipitates were filtered off and recrystallized with ethanol.

The final product purified and verified by spectroscopic method (¹H-NMR, ¹³C-NMR, FT-IR). The urease inhibitory activity of these compounds is under investigation.

Keywords: *H. pylori*; Urease inhibition; Carbamothiol hydrazine.

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Enterosorbent Based on Lignin Hydrolysed and Lactulose: Investigation of its Combined Effect

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21-23 February 2023

Poster: P182

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Abstract:

The method of enterosorption is widely used in the treatment of intoxications caused by the abuse of alcoholic beverages. Enterosorbents based on lignin hydrolysed are able to adsorb different kinds of toxins in the intestine and are widely applied during the treatment of the adults. The combination of an enterosorbent with a pro / prebiotic allows to obtain the maximum therapeutic effect. "Lactofiltrum" is an example of a complex drug combining the properties of an enterosorbent and a prebiotic. The pharmacological effect of the drug "Lactofiltrum" is due to the properties of the active components included in the composition – lignin and lactulose. The effects of this drug consist of normalization of the colon microbiota and decrease in the intensity of endogenous toxic condition. Thus, the aim of the work is to study combined effect of "Lactofiltrum": prebiotic actions and adsorption ability of the drug "Lactofiltrum" in relation to toxic products of ethanol metabolism. Materials and methods. Quantitative assessment of the adsorption activity of the drug was carried out towards acetic acid (one of the products of ethanol metabolism in human body) by acid-base titration. A series of working solutions with different acid concentrations were prepared, then a single dose of the drug "Lactofiltrum", pre-crushed, was added to the solutions. The sample was stirred on an electric stirrer for 30 minutes, after which it was filtered. The aliquot fraction of the filtrate was titrated with a standard alkali solution. The adsorption was calculated as: $A = ((C_0 - C_{eq}) \cdot V) / m$, where C_0 is the initial concentration of acid in the solution, C_{eq} is the equilibrium concentration of acid after adsorption, V is the volume of the solution in which the adsorption was carried out, m is the mass of the adsorbent. To investigate the prebiotic activity model solutions containing lactobacilli, bifidobacteria and test plates were used to determine the total microbial number. Results. Using mathematical processing of experimental adsorption isotherms, it is shown that Freundlich and Langmuirs theories of monomolecular adsorption are applicable to describe the adsorption process. The values of the adsorption parameters are determined. "Lactofiltrum" has a pronounced prebiotic activity: the number of colonies of lactobacilli and bifidobacteria in the medium of the drug after 72 hours increased on average by 3 and 4.2 times, respectively, compared with the control. Conclusion. The data obtained proved the combined effect of the drug "Lactofiltrum". The adsorption activity does not contradict the prebiotic effect of the drug.

Keywords: Enterosorbent; Adsorption activity; Lignin hydrolysed; Intoxication; Prebiotic; Lactulose

A New Model for Investigating Spray Inhalation Toxicity

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21-23 February 2023

Poster: P183

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Abstract:

Acute inhalation toxicity is the total adverse effects caused by a substance following a single uninterrupted exposure by inhalation over 24 hours. Sprays are the most common form of inhalation exposure in daily life. Due to the widespread use of sprays, the possibility of sudden exposure to high concentrations of chemicals and consequently the occurrence of acute toxicity increases. To date, various organizations have developed laboratory set ups to test inhalation toxicities. However, although these models adapt the continuous exposures but are not mimicking the sudden exposures that might result from corrosions, explosions and even household use of sprays. Considering the difference between sudden exposure and acute exposure, it is important to provide a method that specifically predicts the acute toxicity of short acute exposures to sprays. The purpose of this study is to develop such an experimental model. Tar-o-mar insecticide spray of Foman Chemical Company was used as the sample to be tested, and the sprayer with an electric pump was used as the spray nozzle distribution sample. The size and distribution of the particles, after being sprayed by the spray nozzle and insecticide spray, were investigated by fast and sensitive photography methods. This variable was checked in three nozzle modes and in both mist and spray systems, horizontally at different time intervals in a 10-second frame at a distance of 1-50 cm from the breathing chamber. ImageJ software was used to analyze the distribution of particles. Origin Pro software has been used to process the dispersion and particle impact values at various points. Results showed that dispersion model of spray particles are dependent on the size and direction of spraying. In three nozzles horizontal systems at different distances from the breathing chamber, the most exposed for 100% exposure is created at a distance of 40 cm from the spray and at a distance of 10 cm from the nozzle. In this research, the distance of the nozzle from the respiratory chamber is one of the important factors in the exposure and incidence of toxic effects, which should be considered in the design of laboratory models. The results of this study have been used to design a dose-response model in the inhalation toxicity of spray exposure, which can be used with more accuracy and precision than the existing.

Keywords: Toxicity; Inhalation; Spray; Model

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Abdel-Kerim	Karolina	P182
Abdizadeh	Tooba	P156
Adelpour	Tina	O102
Adib	Nadia	P166
Afanasyeva	Yulia	P177
Aghazadeh Shabestari	Farnaz	P133
Ahmadfilab	Parisa	P161
Ahmadi	Mahnaz	P132
Ahmadi	Mahnaz	P145
Akbarzadehlaleh	Parvin	P140
Akhtari	Negin	P139
Alavi	Darya	P112
Alemi	Mehrdad	P158
Alemi	Mehrdad	P159
Alizadeh	Ali Akbar	P134
Altynbek	Dana	O122
Amidi	Salimeh	P161
Amidi	Salimeh	P162
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