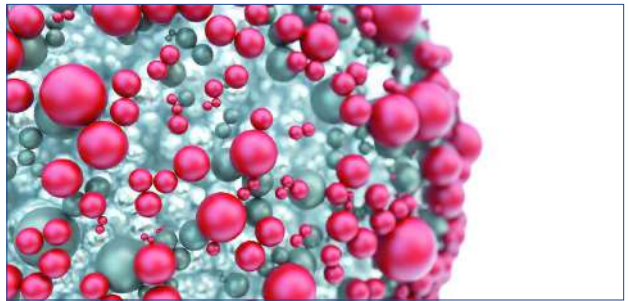

Scientific Tracks & Sessions

April 28, 2022

Pharmaceutical Science 2022



6th International Conference on
Pharmaceutical Science and
Advanced Drug Delivery Systems

April 28, 2022 | Webinar

Novel Drug Delivery System | SARS-CoV-2 | Pharmaceutical Technology | Drug Delivery | Pharmaceutical biotechnology | Drug Discovery and Development



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Session Introduction

Title: Potency of injectable nano formulations as robust anti-bacterial agent to combat bacterial resistance

Sivakumar S Moni | Jazan University | Saudi Arabia

Title: Computational and *In Vitro* experimental investigations reveal anti-viral activity of Licorice and Glycyrrhizin against severe acute respiratory syndrome coronavirus 2

Ahmed Majdi Tolah | King Abdulaziz University | Saudi Arabia

Title: Role of natural substances in countering non alcoholic liver damage in HIFA models.

Tabinda Hasan | Princess Nora bint Abdul Rahman University | Saudi Arabia

Title: Theoretical analysis of metabolic system of an ethanol-neutralizing erythrocyte-bioreactor

Evgeniy Protasov | Ministry of Healthcare | Russia

Title: Development of biotechnical system for automated incorporation of drugs into human erythrocytes

Anna Suvorova | Russian Academy of Sciences | Russia

Title: Ammonium removal by erythrocytes-bioreactors based on glutamate dehydrogenase and alanine aminotransferase

Larisa Koleva | Ministry of Healthcare | Russia

Title: Isolation, structure elucidation and antimicrobial evaluation of natural pentacyclic triterpenoids and phytochemical investigation of different fractions of *Ziziphus spina-christ*

Essam N Ads | Zagazig University | Egypt

Pharmaceutical Science and Advanced Drug Delivery Systems

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Potency of injectable nano formulations as robust anti-bacterial agent to combat bacterial resistance

Sivakumar S Moni*, Muhammad H Sultan, Osama A Madkhali, Mohammed Ali Bakkari and Saad S Alqahtani
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Introduction: Resistance to a wide spectrum of antibiotics and antibacterial agents is prevalent, and it can be induced by a variety of mechanisms, including efflux pumps and exocytosis. Two nano-formulations, nanoparticles, and nano vesicular systems have been constructed, and their physicochemical characteristics have been examined to show their suitability for developing injectable nano formulations. The in vitro anti-bacterial potential was examined to determine the efficacy of injectable nano formulations.

Methods: The nanoparticles and nanovesicles were effectively formulated and characterized physicochemical by zeta potential (ZP), polydispersity index (PDI), particle size distribution, SEM, TEM, XRD and DSC analysis. In vitro agar well diffusion technique was performed to demonstrate the anti-bacterial efficacy against selected human pathogenic bacteria.

Results: Interestingly, both nanoparticles and nanovesicles exhibit unique physicochemical characterization. The injectable

dosage forms were homogenous, and their antibacterial spectrum were demonstrating broad spectrum activity against selected both Gram-positive and Gram-negative bacteria.

Conclusion: The results of the studies showed that injectable nano formulations were successful to target human pathogenic bacteria to combat bacterial resistance.

Speaker Biography

S.M. Sivakumar is an Assistant Professor at the College of Pharmacy, Jazan University, Jazan, Kingdom of Saudi Arabia. He is an active researcher, undergoing many funded projects. His research work is on nano-medicines targeted delivery, drug delivery, and vaccine delivery. His research work extended on newer drug design for the development of antimicrobials, anticancer, and immunomodulatory principles from the seaweed and herbs of the southwestern region of Saudi Arabia. He has more than 50 research and review articles in peer-reviewed journals.

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Computational and *In Vitro* experimental investigations reveal antiviral activity of Licorice and Glycyrrhizin against severe acute respiratory syndrome coronavirus 2

Ahmed Majdi Tolah and et al., Lamy M Altayeb, Thamir A Alandijany, Vivek Dhar Dwivedi, Sherif A El-Kafrawy and Esam I Azhar

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Introduction: Without effective antivirals, the COVID-19 pandemic will likely continue to substantially affect public health. Medicinal plants and phytochemicals are attractive therapeutic options, particularly those targeting viral proteins essential for replication cycle.

Methods: A total of 179 phytochemicals of licorice (*Glycyrrhiza glabra*) were screened and scrutinized against the SARS-CoV-2 main protease (Mpro) with considerable binding affinities in the range of -9.831 to -2.710 kcal/mol. *In vitro* studies demonstrated robust anti-SARS-CoV-2 activity of licorice and glycyrrhizin under different treatment protocols (simulations treatment with viral infection, post-infection treatment, and pre-treatment), suggesting multiple mechanisms for action. Results: The top 10 compounds with the best docking scores, licuraside, glucoliquiritin apioside, 7,30-Dihydroxy-50 - methoxyisoflavone, licuroside, kanzonol R, neoisoliquiritin, licochalcone-A, formononetin, somucronulatol and licoricone, were redocked using AutoDock Vina, yielding -8.7 to -7.3 kcal/mol binding energy against Glycyrrhizin (-8.0 kcal/mol) as a reference ligand. Licorice and glycyrrhizin compounds

inhibited SARS-CoV-2 replication, the half-maximal inhibitory concentration (IC₅₀) of glycyrrhizin was substantially lower than licorice.

Conclusion: Four compounds, licuraside, glucoliquiritin apioside, 7,30-Dihydroxy-50-methoxyisoflavone and licuroside, with glycyrrhizin (reference ligand) were considered for the 100 ns MD simulation and postsimulation analysis which support the stability of docked bioactive compounds with viral protein. This study supports proceeding with *in vivo* experimentation and clinical trials and highlights licorice and glycyrrhizin as potential therapeutics for COVID-19.

Speaker Biography

Ahmed Majdi Tolah is currently an Assistant Professor at the King Abdulaziz University, Faculty of Applied Medical Science, Virology, Rabigh, Saudi Arabia and Researcher at Special Infectious Agents Unit, King Fahd Medical Research Center, Jeddah, Saudi Arabia. Science and Research Branch. He graduated Ph.D. Degree in Microbiology (Virology) in 2019. His research interests are diagnosis and treatment of viruses (SARS-CoV-2, MERS-CoV, Influenza virus and Dengue virus), drug and natural products discovery.

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Role of natural substances in countering nonalcoholic liver damage in HIFA models

Tabinda Hasan

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Non-alcoholic steatohepatitis (NASH), the progressive form of non-alcoholic fatty liver disease (NAFLD), is emerging as the main health problem in industrialized countries. Lifestyle modifications are effective in the treatment of NAFLD; however, the long-term compliance is low. Therefore, several pharmacological treatments have been proposed but none has shown significant efficacy or long-term safety. Natural polyphenols are a heterogeneous class of polyphenolic compounds contained in vegetables, which are being proposed for the treatment of different metabolic disorders.

Although the beneficial effect of these compounds has traditionally related to their antioxidant properties, they also, exert several beneficial effects on hepatic and extra-hepatic glucose and lipid homeostasis. Furthermore, natural polyphenols exert antifibrogenic and antitumoural effects in animal models, which appear relevant from a clinical point of view because of the association of NASH with cirrhosis and hepatocellular carcinoma. Several polyphenols, such as anthocyanins, curcumin and resveratrol and those present in coffee, tea, soy are available in the diet and their consumption can be proposed as part of a healthy diet for the treatment of NAFLD.


Other phenolic compounds, such as silymarin, are commonly consumed worldwide as nutraceuticals or food supplements. Natural antioxidants are reported to have beneficial effects

in preclinical models of NAFLD and pilot clinical trials and thus need clinical evaluation. In this review, we summarize the existing evidence regarding the potential role of natural antioxidants in the treatment of NAFLD and examine possible future clinical applications.

Speaker Biography

Tabinda Hasan is MBBS, MD, PGDHE (higher education), and PhD. (Anatomy), is an Assistant Professor at the Princess Nora bint Abdul Rahman University, Riyadh, Saudi Arabia. She has 12 years of teaching experience in anatomy and is proficient in Cadaveric Dissection and prosection, Video-based case construction in Problem-based learning, Research methodology, Research Ethics, Induced pluripotent stem cell culturing techniques, and Atomic force microscopy. She was awarded by Boston university school of medicine, USA (advancing ethical research award), Marie curie research award in anatomy for 2015 (with 5000 participants from over 80 countries), Stem cell unit, King Saud University, KSA (Effective scientific vocalizations); OSDOW 2011 nominee, Elsevier, Trieste-Italy (women in science for developing world), Faculty of Medicine & Health sciences, Saudi Arabia (excellence in Teaching award). She has headed the scientific committee for 3 consecutive years for the Medical Research Day international conference in Saudi Arabia. She is a renowned author, with 38 Journal publications and 95 citations, 36 conference presentations including Masseurchets -USA, California, Germany, Venice-Italy, Bulgaria, Malaysia, Korea, Greece, Dubai, Abu-Dhabi, Qatar, India, Saudi Arabia, Pakistan. She is a keen researcher and has served as principal investigator in several multinational research projects.

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Theoretical analysis of metabolic system of an ethanol-neutralizing erythrocyte-bioreactor

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Introduction: Erythrocytes-bioreactors (EBRs), containing an artificially built-in metabolic pathway that is absent in a normal erythrocyte, can potentially be used in the treatment of some diseases. They can regulate the concentration of certain target substances in a patient's blood by producing or consuming these substances in reactions of the embedded pathway. EBRs consuming ethanol, methanol, ammonium, asparagine, and other substances have been developed by different scientific groups worldwide. However, most of these bioreactors were ineffective in vitro and in vivo. Many factors can limit the effectiveness of a complex metabolic system like EBR. Mathematical modeling of metabolic systems can help reveal these limitations and turn the EBR development process into an engineering problem.

Methods: Systems of the first-order ordinary differential equations (ODEs) were used to model metabolic systems of various EBRs. The models included equations describing the rate of glycolysis and the pentose phosphate pathway, built-in reactions, and the transport of certain metabolites across the erythrocyte membrane. To analyze the models, numerical solutions of ODE systems, methods of the theory of dynamical systems, and methods of reduction of ODE systems (Tichonov theorem) were used.

Results: Mathematical models of ethanol-neutralizing EBRs based on alcohol dehydrogenase and acetaldehyde dehydrogenase were studied. Pyruvate influx from the external media turned out to be the main limitation of the EBR's efficiency. In the case of lack of pyruvate influx increase of activities of ethanol-consuming enzymes leads

to the disappearance of the steady-state in glycolysis due to a decrease of NAD/(NAD+NADH) value. In normal RBCs this value is maintained near 1 by the NADH oxidation in the reaction catalyzed by lactate dehydrogenase. As NAD is reduced by alcohol dehydrogenase and acetaldehyde dehydrogenase, an increase in their activities leads to a decrease in NAD concentration. The steady-state disappears due to the dependence of the maximum possible rate of glyceraldehyde phosphate dehydrogenase reaction on NAD/(NAD+NADH) value, that leads to accumulation of some metabolites of glycolysis in the cell.

Conclusion: Analysis of mathematical models has shown that ethanol-neutralizing EBRs based on alcohol dehydrogenase and acetaldehyde dehydrogenase are potentially able to decrease ethanol concentration in blood. An increase in the activities of the enzymes of the embedded pathway can lead to the disappearance of the steady-state in glycolysis. Maximum permissible activity depends on the pyruvate influx from the external media.

Speaker Biography

Evgeniy Protasov was born in Stavropol, Russia in 1991. In 2015, he graduated from the Physics Department of Lomonosov Moscow State University. He is a junior researcher at the Center for Theoretical Problems of Physicochemical Pharmacology, Russian Academy of Sciences, and the Dmitriy Rogachev National Medical Research Center of Pediatric Hematology, Oncology, and Immunology, Moscow, Russia.

Interests: biophysics, systems biology, mathematical modeling of metabolic networks, kinetics of enzymes.

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Development of biotechnical system for automated incorporation of drugs into human erythrocytes

Anna Suvorova

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Introduction: Drug delivery using natural biological carriers, especially erythrocytes, is a rapidly developing field. Such erythrocytes carriers (EC) can act as carriers that prolong the drug's action due to its gradual release from the carrier; as bioreactors with encapsulated enzymes performing the necessary reactions, while remaining inaccessible to the immune system and plasma proteases. To date, erythrocytes have been studied as carriers for a wide range of drugs, however, their use in the clinic is limited mainly by the lack of automated drug encapsulation methods.

Methods: To incorporate biologically active drugs into erythrocytes, an automated unit was developed using the method of hypoosmotic flow dialysis. The installation includes a device for washing cells, a dialyzer, peristaltic pumps, sensors for hematocrit, pressure and the presence of liquid in the conductive lines connecting different units of the installation. The operation of the device is controlled by a specially the developed program, which allows the procedure completely automatically under sterile conditions.

Results: Using the developed automated biotechnical system the asparaginase enzyme, which is used in the treatment of leukemia was incorporated into human erythrocytes. Verification of the obtained EC (n=11) showed

the complete sterility of the preparations. The efficiency of enzyme incorporation using the developed setup (the percentage of the enzyme included in erythrocytes) averaged $E=22.5\pm 4.4\%$, and the cell yield (percentage of erythrocytes preserved after the procedure) was equal to $C=55.1\pm 4.6\%$. The relative incorporation efficiency ($R=51.8\pm 9.6\%$) was also evaluated, which is the percentage that the specific activity of the enzyme obtained in erythrocytes is from the maximum possible under given conditions.

Conclusion: The developed automated biotechnical system allows sterile and reproducible incorporation of an enzyme preparation (asparaginase) into human erythrocytes with high efficiency, which exceeds the efficiency of all other currently existing devices for incorporating medicinal compounds into erythrocytes.

Speaker Biography

Anna Suvorova received her master's degree in 2018 from the Bauman Moscow Technical University and is currently a graduate student at the Faculty of Biotechnical Technologies of this university. Her research interests include biotechnology and the development of new instruments for scientific research, in particular, for the creation of new dosage forms for the delivery of medicines.

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Isolation, structure elucidation and antimicrobial evaluation of natural pentacyclic triterpenoids and phytochemical investigation of different fractions of *Ziziphus spina-christi*

Essam N Ads

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Resistance to chemotherapeutic agents and adverse side effects of radiation are problems in clinical cancer treatment. Drugs inspired by natural products constitute many approved drugs for cancer as many as 247 drugs were approved from 1981 to 2019. Therefore, it is of interest to report the cytotoxic effects of *Z. Spina Christi* bark crude extract on human cell lines. *Z. Spina-Christi* possesses significant amounts of diverse phytochemicals, most importantly flavonoids, saponins, tannins, and triterpenes. The bark of *Z. Spina-Christi* has potent biological activities such as antinociceptive, antidiarrheal and antimicrobial activities. Previous reports revealed the biological importance of betulin as it showed adaptogenic, antioxidant, cytotoxic, anti-inflammatory, immune-modulator, and hypolipemic activities. Also, a combination of betulinic acid with anticancer drugs showed induction of apoptosis, caspases, and inhibition of the survival of clonogenic tumor cells. Betulinic acid exerts a plethora of pharmacological properties, especially as anti-inflammatory, antibacterial, and antiviral agents, in addition to its antidiabetic, antimalarial, anti-HIV, and antitumor properties. This study aimed to explore the antimicrobial activity of different fractions of *Z. Spina-Christi* (L.) stem bark, followed by bioassay-guided fractionation and isolation of the major bioactive compounds. Moreover, this study explores the metabolic pattern of different fractions of ZSC-L stem bark using LCHRMS. In the present work, different fractions of *Z. Spina-Christi* L. exhibited a varying degree of antimicrobial activity. Besides, LC-HR-MS analysis was used to identify metabolites of different fractions of *Z. Spina-Christi* L. The results revealed the presence and identification of 36

phytochemical compounds and biological studies carried out on the stem bark of *Z. Spina-Christi* L. Phytochemical investigations led to the isolation of two pure compounds, betulinic acid (C₃₀H₄₈O₃) and betulin (C₃₀H₅₀O₂). The structure of these compounds was determined by IR spectroscopy, mass spectroscopy, ¹H, and ¹³C NMR and confirmed by comparing with the previously reported values. The molecular docking studies on betulinic acid and betulin against enzymes in various microorganisms revealed the potential binding affinity to the site of the appropriate targets. The n-butanol fractions of ZSC- L. have potent antimicrobial activity. Further investigation of the isolated metabolites is required to identify the bioactive compounds responsible for antimicrobial, antioxidant, and cytotoxic effects that may have potential in pharmaceutical and clinical applications.

Speaker Biography

Essam Ads is currently an assistant professor at the forensic medicine institute, ministry of justice. He graduated with (an M.Sc. degree in Organic Chemistry-2001), (a Ph.D. degree in Applied Organic Chemistry-2009) - Department of Chemistry, Faculty of Science, Zagazig University, Egypt. From (2009-2019) Assistant professor of Organic chemistry-Faculty of Science, Hail University, KSA. His research interests focus on Applied Chemistry using the green procedure. Isolation of natural products from different plants is of medicinal importance using different chromatographic techniques and determining their structures using different spectroscopic techniques. To establish the biological activities of these plants and natural products. Also, syntheses of organic compounds using classical and solvent-free conditions (green Chemistry).

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