PEERS ALLEY MEDIA

VIRTUAL EVENT

INTERNATIONAL CONFERENCE AND EXHIBITION ON

THE FUTURE OF PHARMACEUTICS AND NOVEL DRUG DELIVERY SYSTEMS

FUTURE PHARMA 2022

MARCH 28-29
2022

Peers Alley Media
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PROGRAM-AT-A-GLANCE

FUTURE PHARMA 2022

DAY 1

MARCH 28, 2022

Scientific Program

GMT-Greenwich Mean Time

08:45 - 09:00	**Opening Ceremony**

Distinguished Speaker Talks

09:00-09:20	**Title: Macrophages and immune responses in uterine fibroids** **Alessandro Zannotti,** *Polytechnic University of Marche, Italy*
09:20-09:40	**Title: Title: Formulation development of cevimeline hydrochloride mouth dissolving tablets using 2^3 factorial design approach** **Sagar Kothawade,** *Sinhgad Institute of Pharmacy, India*
09:40-10:00	**Title: Study on the effect of an ion channel inhibitor "Fluralaner" on Echinococcus granulosus protoscolices and metacestode layers *in vitro*** **Fatima Zahran,** *Ain-Shams University, Egypt*
10:00-10:20	**Title: Determination of heavy metal, aflatoxin, pesticide residue and microbial content of siddha polyherbal formulation Veppampoo mathirai** **S. M. Chitra,** *Government Siddha Medical College, India*
10:20-10:40	**Title: Determination of zolpidem in plasma using molecularly imprinted polymer solid phase extraction followed by high performance liquid chromatography** **Shabnam Pourmoslemi,** *Hamadan University of Medical Sciences, Iran*
10:40-11:00	**Title: Ziconotide: The revival of an old non-opioid pain reliever** **Georgios K. Matis,** *University Cologne Hospital, Germany*

Refreshment Break 11:00-11:10

Distinguished Speaker Talks

11:10-11:30	**Title: Neural network model for the pharmaceutical plant machine availability prediction** **Deepika Garg,** *G.D. Goenka University, India*

11:30-11:50	**Title: Innovative approach for management of acute poisoning** **Muneera Al-Jelaify,** *King Saud University Medical City, Saudi Arabia*
11:50-12:10	**Title: Physical modification approaches to enhance cell supporting potential of poly (vinyl alcohol)-based hydrogels** **Mahtab Firoozi,** *Yazd University, Iran*
12:10-12:30	**Title: Experimentally designed Tizanidine Hydrochloride aspasomes as nanocarriers for transdermal drug delivery: *In-Vitro* evaluation and *in-Vivo* assessment** **Hadeer A. El-Hashemy,** *National Research Centre, Egypt*
12:30-12:50	**Title: Fever is not a symptom in COVID-19: None of the diseases require fever as its symptom** **K. M. Yacob,** *Marma Health Centre, India*
12:50-13:10	**Title: Identification of generalized peptide vaccine candidates for SARS-COV-2 through computational analysis** **Smarajit Manna,** *Jagadis Bose National Science Talent Search, India*

Lunch Break 13:10-13:50

Distinguished Speaker Talks

13:50-14:10	**Title: The role of synthetic and biological test systems in the development of transdermal drug delivery systems** **E. G. Kuznetsova,** *Ministry of Health of the Russian Federation, Russia*
14:10-14:30	**Title: Cell penetrating sequential oligopeptide carrier: A multivalent molecule for intracellular targeting and biomedical applications** **Evgenia Fotou,** *University of Ioannina, Greece*
14:30-14:50	**Title: The importance of doctor-patient relationship regarding medical malpractice claims** **Anna Wszołek,** *Jagiellonian University, Poland*
14:50-15:10	**Title: Prostate cancer and cholesterol metabolism** **Monika Ulamec,** *University of Zagreb, Croatia*

15:10-15:30	**Title: Identification of specific Bromodomain family members as potential therapeutic targets in stem cell-like tumors** **Patrycja Czerwińska,** *Poznan University of Medical Sciences, Poland*

Refreshment Break 15:30-15:40

15:40-16:00	**Title: Preventing COVID-19 through Indian spices** **Amit Jaiswal,** *Friedrich Schiller University, Germany*
16:00-16:20	**Title: Emulsion adjuvants in vaccines stepping up to meeting the pandemic challenge** **Rushit Lodaya,** *GSK – Rockville Center for Vaccines Research, USA*

Keynote Talks

16:20-16:50	**Title: Photodynamic therapy - *in vitro* and *in vivo* bladder cancer models by using novel photosensitizers** **Odrun A. Gederaas,** *Norwegian University of Science and Technology, Norway*
16:50-17:20	**Title: The roles of Pten-NOLC1 gene fusion in human cancers** **Jianhua Luo,***University of Pittsburgh School of Medicine, USA*
17:20-17:50	**Title: mRNA and exosome-mediated directed gene therapy of cancer with no side effects** **A. C. Matin,** *Stanford University School of Medicine, USA*

Panel Discussion

End of Day 1

DAY 2

MARCH 29, 2022

Scientific Program

GMT-Greenwich Mean Time

Distinguished Speaker Talks

09:00-09:20	**Title: Novel voltage gated calcium channel blocker inhibits the proliferation of oral squamous cell carcinoma** **Rajdeep Chakraborty,** *Macquarie University, Australia*
09:20-09:40	**Title: A systematic review of literature of *in vitro* and *in vivo* antiplasmodial, antimalarial activities of African medicinal plants** **Faham Khamesipour,** *Shahid Beheshti University of Medical Sciences, Iran*
09:40-10:00	**Title: Understanding transcriptomics of neurodevelopmental disorders: A computational approach** **Prachi Srivastava,** *Amity University, India*
10:00-10:20	**Title: Hansen solubility theory in the extraction of policosanol from sugarcane wax** **Eduardo Hernández Ramos,** *Cuban Research Institute of Sugarcane Derivatives, Cuba*
10:20-10:40	**Title: The neuroprotective effect of artemisinin and its analogs and their implication in the treatment of ischemic stroke** **Wenhua Zheng,** *University of Macau, China*
10:40-11:00	**Title: Does fever increase or decrease blood circulation?** **K. M. Yacob,** *Marma Health Centre, India*

Refreshment Break 11:00-11:10

Distinguished Speaker Talks

11:10-11:30	**Title: Effects of replacing fishmeal with dietary dried distillers grains with solubles on growth, serum biochemical indices, antioxidative functions, and disease resistance for Litopenaeus vannamei juveniles** **Gyan Watson Ray,** *Guangdong Ocean University, China*

11:30-11:50	**Title: Complex of breast milk antimicrobial peptides as a source of natural antibiotics** **Tatiana Kolyganova,** *Sechenov University, Russia*
11:50-12:10	**Title: Protein network analysis to prioritize key genes in amyotrophic lateral sclerosis** **Shazia Haider,** *Jaypee Institute of Information Technology, India*
12:10-12:30	**Title: The therapeutic potential of herbal and nano-based herbal therapy against ovarian cancer: New insight into the current evidence** **Reza Arefnezhad,** *Shiraz University of Medical Sciences, Iran*
12:30-12:50	**Title: Anti-integrins: Is there a future** **Dermot Cox,** *Royal College of Surgeons, Ireland*

Lunch Break 12:50-13:40

13:40-14:00	**Title: Applications of Bayesian analysis to proof-of-concept trial planning and decision making** **René Kubiak,** *Sanofi, Germany*
14:00-14:20	**Title: *In vivo* acute toxicity of the biosurfactant mannosylerythritol lipids to swiss mice after intraperitoneal administration** **Cristiano José De Andrade,** *Federal University of Santa Catarina, Brazil*

Keynote Talk

14:20-14:50	**Title: New methodologies for population-based rare disease epidemiology: Cost-effective/ multi-country examples** **Jack Ray Gallagher,** *Clarity Pharma Research LLC, USA*

Panel Discussion

End of Day 2

BOOKMARK YOUR DATES

International Conference
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KEYNOTE PRESENTATIONS

DAY 1

PEERS ALLEY MEDIA

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FUTURE PHARMA 2022

BIOGRAPHY

Odrun A. Gederaas, Associate Professor/Researcher obtained her Dr. Philos. degree in medical technology (2001), Norwegian University of Science and Technology (NTNU), in collaboration with University of Leiden (The Netherlands) and the Norwegian Radium Hospital, Norway. The interdisciplinary fields in photodynamic therapy (PDT) were developed during her post-doctoral fellows (2002-2006) including research stays in USA (Ohio and Irvine) and Austria (Salzburg). Novel technologies, animal models, patent and prizes have been established in collaboration with pharmacology companies. Her research group in PDT (2009-2017) were connected to fields of analytical chemistry, cellular biology, and human treatments. Co-author of about 50 publications.

Odrun A. Gederaas

Department of Physics, Norwegian University of Science and Technology, Norway

Photodynamic therapy - *in vitro* and *in vivo* bladder cancer models by using novel photosensitizers

Photodynamic therapy (PDT) is an effective treatment for both malignant and non-malignant diseases, and new photosensitizers / chromophores are studied by confocal imaging and biological techniques determining cell survival with/without light. During PDT the activated PS transfers energy to nearby oxygen molecules, generating singlet oxygen ($^1O_2$) resulting in oxidative stress (ROS), which further elicit cell death by necrosis and apoptosis. Protoporphyrin IX (PpIX), is an efficient and widely used PS for bladder superficial bladder cancer treatment; either endogenously produced in the cancer cells by e. g. aminolaevulinic acid (ALA) or exogenously added as e. g. hexyl-ALA. The effects *in vitro* and *in vivo* are present by using an orthotopic rat bladder cancer model; also included photochemical internalization (PCI). This is a new strategy for local enhancement of various types of drug molecules by employing a photosensitising compound and illumination of a diseased area in the body. The possibility of using PCI to enhance effects of the cytotoxic drug bleomycin is investigated, together with photophysical determinations and outlines of a treatment for intravesical therapy of bladder cancer. *In vitro* experiments indicate that employment of PCI technology using the novel photosensitizer $TPCS_{2a}$® enhance cytotoxic effects of bleomycin in bladder cancer cells. Furthermore, experiments in an orthotopic *in vivo* bladder cancer model show effective reduction in both necrotic area and bladder weight after $TPCS_{2a}$ based photodynamic therapy (PDT). The tumor selectivity and PDT effects may be sufficient to destroy tumors without damaging detrusor muscle layers. Our results present a possible new treatment strategy for non-muscle invasive bladder cancer, with intravesical instillation of photosensitizer and bleomycin followed by illumination through an optic fiber by using a catheter.

BIOGRAPHY

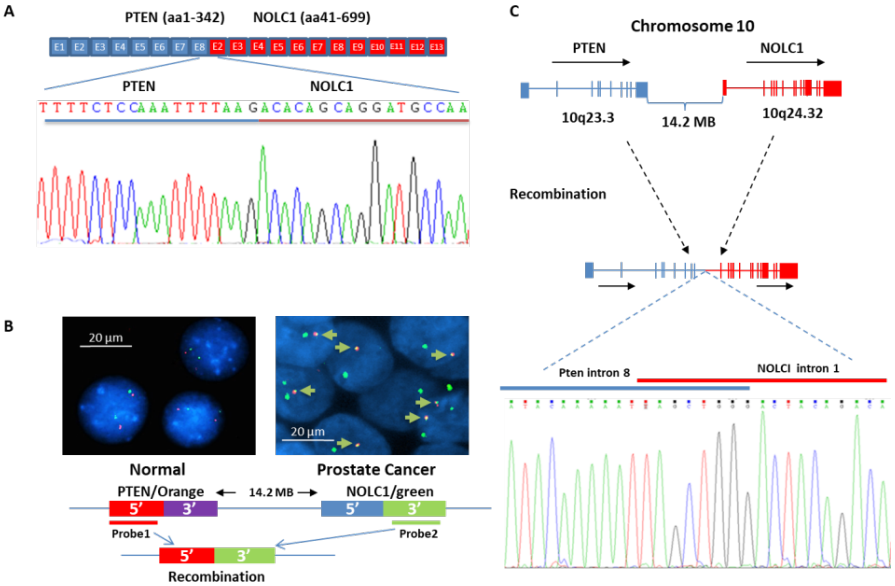
Jianhua Luo has been studying molecular mechanisms of human malignancies in the last 33 years. Currently, he is a Professor of Pathology and Director of High Throughput Genome Center at University of Pittsburgh. In the last 28 years, Dr. Luo has been largely focusing on the genetic and molecular mechanism of human prostate and hepatocellular cancers. He proposed prostate cancer field effect in 2002. He is one of the pioneers in utilizing high throughput gene expression and genome analyses to analyze field effects in prostate cancer and liver cancer. He is also the first in using methylation array and whole genome methylation sequencing to analyze prostate cancer. He and his colleague helped to develop an ultra-low error synthetic long-read sequencing technology called LOOPSeq that can be utilized to quantify mRNA isoforms and mutation isoform distributions. Recently, his group discovered 18 novel fusion genes in prostate, liver and colon cancers. Overall, these findings advance our understanding of how cancer develops and behaves, and lay down the foundation for better future diagnosis and treatment for human malignancies.

Jianhua Luo

Department of Pathology, University of Pittsburgh School of Medicine, USA

The roles of Pten-NOLC1 gene fusion in human cancers

Inactivation of Pten gene through deletions and mutations leading to excessive pro-growth signaling pathway activations frequently occurs in cancers. Here, we report a Pten derived pro-cancer growth gene fusion Pten-NOLC1 originated from a chr10 genome rearrangement and identified through a transcriptome sequencing analysis of human cancers. Pten-NOLC1 fusion is present in eight different types of primary human cancer samples and cancer cell lines from different organs. The product of Pten-NOLC1 is a nuclear protein



that interacts and activates the promoters of EGFR, c-MET, and their signaling molecules. Pten-NOLC1 promotes cancer proliferation, growth, invasion, and metastasis, and reduces the survival of animals xenografted with Pten-NOLC1-expressing cancer cells. Genomic disruption of Pten-NOLC1 induces cancer cell death, while genomic integration of this fusion gene into the liver coupled with somatic Pten deletion produces spontaneous liver cancers in mice. Our studies indicate that Pten-NOLC1 gene fusion is an important driver for human cancers.

BIOGRAPHY

A.C. Matin, Ph.D worked as a Professor, Emeritus of Microbiology & Immunology in the Department of Microbiology & Immunology at Stanford University School of Medicine.

A. C. Matin

Professor of Microbiology & Immunology, Stanford University School of Medicine, USA

mRNA and exosome-mediated directed gene therapy of cancer with no side effects

Chemotherapy with no or minimal side effects is an urgent need. One means of attaining it is through Gene-Delivered Prodrug Therapies (GDEPTs). Prodrugs are harmless until activated by a bacterial or viral gene product; they can kill tumors without side effects if the activating gene is specifically delivered to cancer. Previous GDEPT approaches have been hampered from low gene delivery and duration of expression; insufficient bystander effect; use of viruses as gene delivery vehicles; and the need to inject the gene directly into the tumor – the latter minimizes GDEPT applicability, since many cancers, particularly cancer metastases, are not amenable to direct gene injection. My collaborators and I have addressed these problems. The use of the prodrug CNOB (C16H7CIN2O4) that we discovered facilitated this because its activated drug MCHB (C16H9CIN2O2) can be quantitatively visualized in living mice; and by using exosomes (EVs) for gene delivery. Recently, we have enhanced the clinical transfer prospect of this approach by:

(i) use of the prodrug CB1954 (tretazicar) for which safe human dose is established, and our humanizes and improved bacterial enzyme, HChrR6; (ii) using HChrR6 mRNA instead of DNA for gene delivery; and (iii) loading exosomes with *in vitro* transcribed HChrR6 mRNA without using potentially harmful plasmids. This loading required several steps. mRNA being unstable, we ensured its functionality for tretazicar activation at each step. Besides tretazicar, HChrR6 can convert CNOB into MCHB, which is easily visualizable through its fluorescence. This enabled us to ascertain HChrR6 mRNA translated product's competence for tretazicar activation by monitoring its ability to generate fluorescence from CNOB. Systemic administration of the loaded exosomes that displayed an anti-HER2 single-chain variable fragment and that of tretazicar killed HER2+ breast cancer xenografts in athymic mice. This occurred without injury to other organs. This, along with the elimination of the need for direct gene injection into the tumor, moves GDEPT closer to clinical transfer. This approach can treat any disease in which a receptor/ligand is overexpressed.

SCIENTIFIC ABSTRACTS

DAY 1

PEERS ALLEY MEDIA

Virtual Event

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Macrophages and immune responses in uterine fibroids

A. Zannotti [1,2], S. Greco[2], P. Pellegrino[2], F. Giantomassi[3], G. Delli Carpini[1], G. Goteri[3], A. Ciavattini[1] and P. Ciarmela[2]

[1]Department of Specialist and Odontostomatological Clinical Sciences, Polytechnic University of Marche, Italy
[2]Department of Experimental and Clinical Medicine, Polytechnic University of Marche, Italy
[3]Department of Biomedical Sciences and Public Health, Polytechnic University of Marche, Italy

Uterine fibroids represent the most common benign tumors of the uterus. They are considered a typical fibrotic disorder. In fact, the extracellular matrix (ECM) proteins—above all, collagen 1A1, fibronectin and versican—are upregulated in this pathology. The uterine fibroids etiology has not yet been clarified, and this represents an important matter about their resolution. A model has been proposed according to which the formation of an altered ECM could be the result of an excessive wound healing, in turn driven by a dysregulated inflammation process. A lot of molecules act in the complex inflammatory response. Macrophages have a great flexibility since they can assume different phenotypes leading to the tissue repair process. The dysregulation of macrophage proliferation, accumulation and infiltration could lead to an uncontrolled tissue repair and to the consequent pathological fibrosis. In addition, molecules such as Monocyte Chemoattractant Protein-1 (MCP-1), Granulocyte Macrophage-Colony-Stimulating Factor (GM-CSF), Transforming Growth Factor (TGF-β), activin A and Tumor Necrosis Factor-alfa (TNF-α) were demonstrated to play an important role in the macrophage action within the uncontrolled tissue repair that contributes to the pathological fibrosis that represents a typical feature of the uterine fibroids.

Biography

Alessandro Zannotti received his Master degree in Molecular and Applied Biology from Polytechnic University of Marche (UNIVPM), Ancona, Italy in 2017. He currently attends the last year of the Ph.D. course in Biomedical Sciences at UNIVPM. He spent a period of study at Life and Health Sciences Research Institute (ICVS), at University of Minho, Braga, Portugal within his Ph.D. internship. His Ph.D. research project is focused on the morphological and molecular characterization of benign leiomyoma and malignant leiomyosarcoma with the aim of identifying potential markers to discriminate them. In particular he studies Raf-1 kinase inhibitor protein (RKIP).

Formulation development of cevimeline hydrochloride mouth dissolving tablets using 2^3 factorial design approach

Sagar Kothawade
Sinhgad Institute of Pharmacy, India

In the present work, the mouth dissolving tablets of cevimeline hydrochloride were prepared to target those patients suffering from Sjogren syndrome, due to this syndrome patient faces problems such as difficulty in swallowing tablets or capsules because of dryness in mouth, resulting in noncompliance and ineffective therapy. Mouth dissolving tablets were prepared by direct compression method. The preliminary trial batches were formulated with three super-disintegrant viz. crospovidone, sodium starch glycolate, croscarmellose sodium in different concentration along with pearlitol SD 200 alone and in combination with microcrystalline cellulose (Avicel102). The prepared batches were evaluated for weight variation, hardness, thickness, mechanical strength, wetting ability, disintegration time and in vitro drug release. Amongst all four-formulation batches, batch no A4 containing crospovidone 8 mg, mannitol & MCC in the ratio of 10:1 has shown disintegration time of 8 seconds along with 96% drug release within 30 min. The compatibility study of drug and excipients was carried out by using FTIR and DSC. Based on the results, trial A4 was selected for further optimization by using 23 factorial design. Among all trials generated by 23 factorial design, D4 shows most satisfactory result like disintegration time about 8 sec and drug release 98% in 30 min, hence formulation D4 considered as optimized formulation.

Biography

Sagar Kothawade completed his Master of Pharmacy with 2+ years experience in formulation R&D of solid oral dosage forms.

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Study on the effect of an ion channel inhibitor "Fluralaner" on Echinococcus granulosus protoscolices and metacestode layers *in vitro*

Fatima Zahran, Hayam Mohamed Ezz El-Din and **Mai Abdel Sameaa Shehata**

Faculty of Medicine, Ain-Shams University, Egypt

Hydatid disease has a great impact on public health, causing high morbidity and mortality. Main lines of treatment include surgery, which mostly requires the installation of a scolicidal agent into hydatid cysts to prevent dissemination. Alternatively, medical treatment involves the use of benzimidazole drugs; however, the results are not satisfactory, and new drug compounds are urgently needed. Fluralaner is a potent inhibitor of GABA gated chloride channels and L-Glutamate-gated Chloride channels (GluCls) providing immediate and persistent flea, tick and mite control in dogs after a single oral dose. Researches previously identified different genes encoding ion channels in Echinococcus granulosus, making ion channel inhibitors a promising target for treating hydatid disease. Thus, the present study aimed to evaluate the effect of fluralaner on protoscolices and metacestode layers. Parasite materials (Protoscolices, Metacestodes layers) were exposed to different concentrations of the drug ranging from "12.5–100 ug/ml" and examined for viability after 1, 6 and 24 h. Morphological and ultrastructural alterations were recorded by both light and electron microscopies. Immunohistochemical staining confirmed caspase-3 activation as an indicator of apoptosis- induced therapy. The treated protoscolices and metacestode layers showed loss of the viability, the formation of vacuoles and lipid droplets, separation of the germinal layer, and damage in the laminated layer; apoptosis was prominent after treatment. These findings revealed that fluralaner has a potent scolicidal activity and suggested its therapeutic potential against hydatid disease. Further evaluations for animals and human use in the treatment and prevention of hydatid disease are needed.

Biography

Fatima Zahran obtained her master's degree in Medical Parasitology in 2011 and MD degree in Medical Parasitology in 2016 from the Faculty of Medicine, Ain-Shams University. I have been working at Ain shams university from 2008 up till now. I am currently working as a lecturer and head of the parasitology department in the Faculty of Medicine, MTI University. I have completed a course offered by Ain shams University, Middle East North Africa FAIMER Regional Institute as a Certified Assessor in Health Professions Educations. I held the position of Vice-Head of the control unit in the Faculty of Medicine, MTI University. My main Interest in Research is the epidemiology of diseases, new diagnostic methods, and new therapeutic modalities.

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Determination of heavy metal, aflatoxin, pesticide residue and microbial content of siddha polyherbal formulation *Veppampoo mathirai*

Dr. S. M. Chitra and **Dr. N. Anbu**

Department of Post Graduate Maruthuvam, Government Siddha Medical College, India

Aim: The polyherbal siddha formulation Veppampoo mathirai is effective in regulating blood pressure but its safety is not known. The heavy metal, aflatoxins, pesticide residue, microbial count have not been evaluated so far. The current study evaluated the above parameters. The present study was aimed to evaluate the safety parameters (heavy metal, aflatoxin, pesticide residue and microbial profile) of Veppampoo mathirai and the objective was to determine whether the above parameters of VPM were within normal limits as per AYUSH guidelines.

Materials and Methods: According to AYUSH [Ayurveda, yoga, unani, siddha, naturopathy] Pharmacopoeial laboratory for Indian medicine (PLIM) guidelines, the formulation was evaluated for its safety parameters at Noble research solutions, kolathur, Chennai, accredited with ISO 9001: 2015.Atomic Absorption Spectrometer (AAS) was used for testing heavy metals and aflatoxins were tested using Thin Layer Chromatography (TLC). The Pesticide residues content was estimated using GC/MS technique and microbial content by pour plate method.

Results: The study revealed presence of heavy metals mercury, arsenic, lead and cadmium within the recommended limit as per AYUSH Pharmacopoeial Laboratory for Indian Medicine Guidelines whereas presence of Aflatoxin, pesticide residues and microbes were absent in the sample which showed the formulation Veppampoo mathirai (VPM) was free from toxicity.

Conclusion: VPM showed heavy metal content below the permissible limit as per PLIM guidelines of AYUSH. Aflatoxins and pesticide residue were not detected while the microbes and specific pathogens were absent in the current batch of VPM. Hence, the present study ensures the formulation was safe for therapeutic use.

Biography

S.M.Chitra completed her under graduation on 1996 and Post-Graduation on 2006 at Government Siddha Medical college, Arumbakkam, Chennai – 106, Tamil Nadu in which working as an Assistant professor since 2011. She had joined Tamil Nadu Government service on 2000 and worked at clinical settings for 10 years in various Government hospital centers. At present, she is pursuing PhD study at The Tamil Nadu Dr. MGR Medical University, Guindy, Chennai. For postgraduate students, she was taking Siddha Medicine and Research Methodology subjects and guiding in their minor project and post graduate thesis. She had done a clinical Covid study during first lock down period on June-July 2020 in collaboration with Omandurar Government Medical college, Chennai. It was a Randomized controlled study with Siddha and modern medicine as an integrated approach and published in International Journal, Journal of Ayurveda and Integrative medicine (JAIM) which she considered it as a remarkable one. She was passionate towards research and article writing. As far as now she had Published 17 papers.

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Determination of zolpidem in plasma using molecularly imprinted polymer solid phase extraction followed by high performance liquid chromatography

Shabnam Pourmoslemi and **Zinat Alimohammadi**

Department of Pharmaceutics, Hamadan University of Medical Sciences, Iran

Improper use of common and easily available drugs such as hypnotics has become a pervasive problem worldwide. Zolpidem, one of the most widely used hypnotics is mainly characterized for its rapid absorption and short half-life [1]. In spite of being highly beneficial in treatment of insomnia, zolpidem use is associated with serious adverse effects [2]; it is also an important drug in forensic medicine as a drug of abuse or in drug-facilitated crimes [3,4]. Development of validated analysis methods for determining drugs with risk of inducing serious adverse effects or abuse in biological samples is of great importance.

This study aimed to develop a sensitive and accurate method for determination of zolpidem in human plasma. A novel Molecularly Imprinted Polymer-Solid Phase Extraction (MIP-SPE) method was used for selective extraction of zolpidem. Polymerization and extraction procedures were optimized to obtain highest extraction of zolpidem from plasma. A HPLC-fluorescence detector method was developed and validated for analysis of the extracted zolpidem.

The method was linear in the range of 10-100 ng/ml (R2=0.9992) with RSD values in the range of 0.45-2.86% and LOD and LOQ of 0.34 and 1.04 ng/ml, respectively. Extraction and analysis of zolpidem from spiked human plasma samples determined zolpidem with more than 90% recovery. The developed method was successfully used to construct the plasma concentration profile of zolpidem for a volunteer after taking single oral dose of zolpidem, with a great similarity with plasma concentration profiles obtained using other sensitive analysis methods like LC-MS/MS [5].

It can be concluded that the method developed in this study can be utilized to determine zolpidem in human plasma and other biological samples with advantages like accessible requirements and providing precise and accurate results.

References:

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5. Piotrowski, P., Bosian, S., Sliwka, K., Buszewski, B. Simultaneous analysis of zolpidem and its metabolite in whole blood and oral fluid samples by SPE-LC/MS for clinical and forensic purposes. Advances in Medical Sciences, 2015. 60(1): p. 167-172.

Biography

Shabnam Pourmoslemi working as Assistant Professor in Food & Drug Control at School of Pharmacy, Hamadan University of Medical Sciences for the past five years, I am graduated from School of Pharmacy, Tehran University of Medical Sciences in both Pharm.D. and PhD degrees. Research has also been a favorite part of my academic career. My efforts have been in diverse areas to develop technologies that diagnose and treat diseases. My research activities are mainly in the field of inorganic nanotechnology and its biomedical applications, novel pharmaceutical dosage forms development, pharmaceuticals analysis method development and quality control of food and pharmaceuticals.

Ziconotide: The revival of an old non-opioid pain reliever

Georgios K. Matis

Department of Stereotactic & Functional Neurosurgery, University Cologne Hospital, Germany

Ziconotide is a synthetic, water-soluble cone snail venom-derived peptide with a molecular weight of 2,639 Daltons. It is a nonopioid analgesic that selectively binds to N-type voltage-sensitive calcium channels on primary nociceptive afferent nerves in the dorsal horn of the spinal cord. This mechanism releases analgesic neurotransmitters into the synaptic gap and subsequently blocks pain signal transmission. Ziconotide does not easily cross the blood-brain barrier, instead revealing its highly potent antinociceptive effect only after intrathecal administration. Because it has a narrow therapeutic window, careful dose titration, and a lag time to allow for onset (and offset) of analgesia and adverse effects are required. The presentation will focus on a recently published consensus proposal and highlight the potential of this drug as well as the areas where additional experience is needed.

Biography

Georgios K. Matis is a senior consultant for neurosurgery. He leads the chronic pain / spasticity sector of the Department of Stereotactic & Functional Neurosurgery in the University Hospital of Cologne. He has been trained in Greece, USA, Switzerland, and Germany.

He is a member of two medical associations (Thessaloniki, Greece & North Rhine, Germany) and also a member of the German Neuromodulation Society (DGNM) and the International Neuromodulation Society (INS).

He serves as reviewer for many international journals and is Editorial Board member for Neuromodulation: Technology at the Neural Interface and Interventional Pain Medicine and Neuromodulation. He holds the position of Editor-in-Chief of the Internet Journal of Neurosurgery. Dr. Matis has published many articles in Greek and international Pubmed-indexed journals and hold many lectures as invited speaker in numerous international congresses and webinars. At the same time, he is Public Education Committee member of the International Neuromodulation Society.

He is involved in many international clinical studies and has been active as instructor for many colleagues in Germany and abroad. He is also an active member of the medical advisory board of the German CRPS Support Group and member of several online consultation platforms. He is actively involved in social media trying to raise awareness about spinal cord stimulation and neuromodulation.

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Neural network model for the pharmaceutical plant machine availability prediction

Deepika Garg
School of Engineering, GD Goenka University, India

In a pharmaceutical plant industry scenario, the machine availability play a vital role to maximize the manufacturing pharmacy product output. In this paper, the Artificial Neural Networks (ANNs) based information processing algorithm has been implemented, and found suitable to predict machines availability as an optimal function. The input data of manufacturing machines availability for ten years are acquired from the industry management and analyzed. The pharmaceutical plant data corresponding to different values of repair and failure rates of different subsystems are analyzed with the help of validated neural network value of availability. Other elements of the trained ANNs comprises of 50 neurons in input layer, 10 neurons in first hidden layer, 10 neuron in second hidden layer and 1 neuron in output layer. This configuration of ANNs approach developed in this research allowed simplifying computational complexities of conventional approaches to solve a large plant machines availability problem. The ANNs methodology in the paper permitted making no assumption, no explicit coding of the problem, no complete knowledge of system configuration, only raw input and clean data found to be sufficient to determine the value of machine availability function for different value of failure and repair rates considered in the paper. Therefore, in this paper a unique configuration of ANNs model is developed that predict machines availability efficiently compared to conventional algorithmic computing methods used today. The results tabulated in the paper are useful for the plant leadership, as the value of failure and repair rates of various subsystems can be fine-tuned at a require clear-cut level to achieve higher availability, and avoid considerably loss of production, loss of man power, and by-pass complete breakdown of concerned system.

Biography

Deepika Garg is an Associate Professor of Mathematics at GD Goenka University, Gurugram, India. She received her PhD degree from National Institute of Technology, Kurukshetra, India. She has more than 15 years of experience in academics and research. Her area of specialization is Reliability Engineering, Heuristics Algorithm, Evolutionary Optimization, Swarm Intelligence, and Neural Network. She has published more than 30 research papers in reputed national and international journals. She has organized a number of Faculty Development Programs and Seminars / Workshops and presented her research papers.She is the author/co-author of 2 books including Reliability Technology Theory and Application 3rd Editions (I. K. International Publisher House Pvt. Ltd., India). She has supervised 4 Ph.D. students in the field of Reliability Engineering, Heuristics Algorithm, and Evolutionary Optimization. She is a reviewer and editorial board member of various scopus indexed journals.

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Innovative approach for management of acute poisoning

Muneera Al-Jelaify and **Suliman Al-Homidah**

King Saud University Medical City, Kingdom of Saudi Arabia

Acute poisoning is a widespread emergency that mandates early management decisions for optimal outcomes. An individualized approach is an ideal way to provide those outcomes. Promoting awareness among healthcare professionals managing acute poisoning about the importance of incorporating the pharmacokinetics and following certain criteria to consider interventions like activated charcoal, antidote, or specific investigations may improve their risk assessment strategies and management plans.

The objective of this quick review is to address the innovative aspects that should be considered to develop a customized care plan for poisoning victims. Our opinions as experts from King Saud University (KSU) Drug and Poison Information Center (DPIC) were considered in the review.

Biography

Muneera Al-Jelaify is currently a senior pediatric clinical pharmacist specialized in pediatric intensive care unit services and working as a poisoning/toxicology information specialist in King Khalid University Hospital, King Saud University Medical City in Riyadh, Saudi Arabia. Muneera received her bachelor and master degrees in clinical pharmacy from King Saud University. She is a board certified pediatric pharmacy specialist by the American Board of Pharmacy Specialties. Muneera published a number of papers in peer reviewed Journals that include reviews, case series and reports and clinical practice guidelines and presented various academic as well as research-based topics at several events. She is collaborating with pharmacy colleges to train under and post graduates and appointed as adjunct clinical assistant professor by Pharmacy College at King Saud University. Muneera received a National Patient Safety Award form Saudi Patient Safety Centre in 2019 as a recognition for her work as patient safety advocate.

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Physical modification approaches to enhance cell supporting potential of poly (vinyl alcohol)-based hydrogels

Mahtab Firoozi[1,2], Mehdi Entezam[1], Elahe Masaeli[2] and **Mohammad Hossein Nasr-Esfahani[2]**

[1]Department of Chemical and Polymer Engineering, Yazd University, Iran

[2]Department of Cellular Biotechnology, Royan Institute for Biotechnology, Iran

PVA-based hydrogels which apply in tissue engineering and regenerative medicine commonly need further modification for favorable and targeted biological applications. moreover, PVA is difficult to cell adhesion and spreading owing to an intrinsic super-hydrophobicity, lack cell-signaling and cell-interactive motifs. In this study, the effect of different physical modification methods on adhesion behavior and cytoskeleton morphology of seeded cells on PVA hydrogel was exactly compared. PVA-modified hydrogels consisting of PVA/Poly (R-3-hydroxybutyrate) (PHB), PVA/Extracellular Matrix (ECM) and PVA/PHB/ECM were fabricated by freeze-thaw cross-linking step and additive materials effect on cell supporting potential of the hydrogels was investigated. The crystalline nature of PVA is also of interest for forming crystalline zones as physical cross-linked network in a hydrogel, which can be developed by repeated simple freeze-thaw cycles. As, limited cell attachment and spreading were observed on pure and ECM-coated PVA hydrogels, air plasma surface modification has been performed on creating functional groups to promote cell attachment. Attenuated Total Reflection Fourier

Transform Infrared (ATR-FTIR) spectroscopy revealed the presence of some reactive bonds such as carbonyl on pure and amide on ECM-coated PVA after plasma exposure. Atomic Force Microscopy (AFM) also proved increased roughness of hydrogel surface due to the plasma treatment. Plasma modification positive effect on cytoskeleton arrangement of cultured equine adipose derived stem cells (eASCs) was then confirmed by DAPI/phalloidin staining and Scanning Electron Microscopy (SEM) imaging. Consequently, among different physical modification approaches, coating with ECM fallowed by air plasma treatment not only the number of attached cells increased, but also cells totally spread throughout the scaffold and extended their actin filaments. Thus, this combined modification method can be utilized to improve initial attachment and subsequent phenotype of cultured cells on PVA hydrogels for tissue engineering applications.

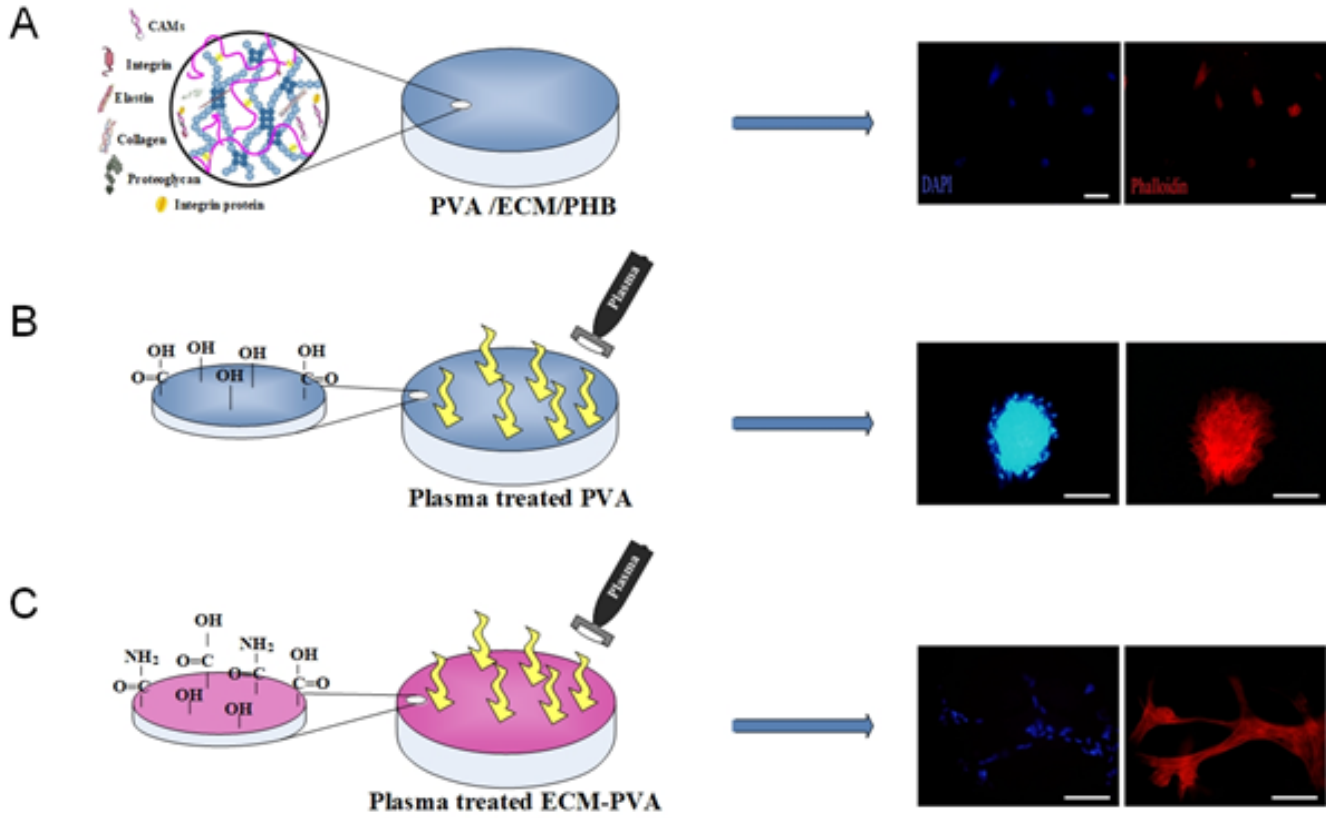

Figure 1. DAPI/phalloidine staining images, illustrating nuclei (blue) and actin cytoskeleton filaments (red) of cultured cells on PVA/ECM/PHB (A), plasma treated PVA (B) and ECM-PVA (C) hydrogels.

Biography

Mahtab Firoozi is a M.S student in Polymer Engineering at Yazd University. She holds her master degree from a joint program at Yazd University & Royan Institute. Her work focuses on the applications of PVA-based hydrogels in tissue engineering. In particular, she has studied initial cell attachment and mechanical properties improvement of PVA hydrogels by using different solutions, especially applying nanofibers and plasma.

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Experimentally designed tizanidine hydrochloride aspasomes as nanocarriers for transdermal drug delivery: *In-vitro* evaluation and *in-vivo* assessment

Hadeer A. El-Hashemy[1], Rawia M. Khalil[1], Ahmed Abdelbary[2], Silvia Kocova El Arini[1], Mona Basha[1] and **Faten Farouk[3]**

[1]*National Research Centre, Egypt*

[2]*Department of Pharmaceutics, Cairo University, Egypt*

[3]*Department of Pharmaceutical Chemistry, Ahram Canadian University, Egypt*

In the present study, aspasomes were developed to enhance the in-vitro dissolution and the in-vivo performance for tizanidine hydrochloride (TZN), a skeletal muscle relaxant with low oral bioavailability.

A Full factorial experimental design was applied to statistically optimize the formulation variables: the amount of drug, amount of ascorbyl palmitate (AP) and the amount of span 60 on the entrapment efficiency, the vesicle size and the in-vitro release. Aspasomal formulation (TZN-AS 6) composed of 20 mg TZN, 50 mg AP and 50 mg span60 was obtained by employing the desirability function of Design-Expert® software. Findings: The optimal formula exhibited an encapsulation efficiency of 95.0 % and smooth surface with particle size 191.8 nm. In addition, skin

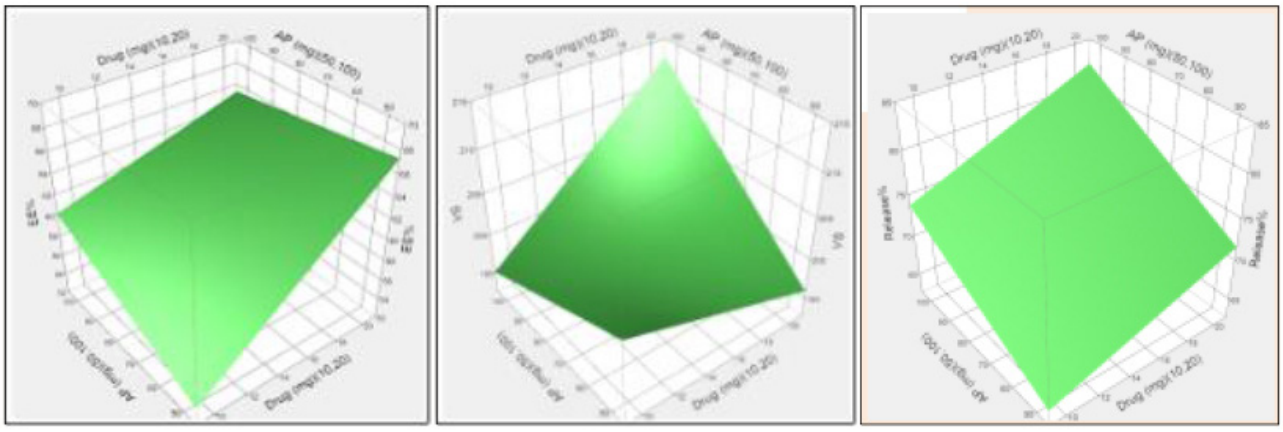

Fig. 1: 3-D surface profilers for EE % (Y1) at two factors interaction

permeation profile was obtained using static vertical diffusion Franz cells and hairless mouse skin treated with TZN-AS 6 aspasomes 0.2% (w/w) TZN, and compared with unformulated drug. Ex-vivo drug permeation across rat skin for TZN-AS 6 showed a superior skin permeation potential with the highest enhancement ratio value compared to the unformulated drug (ER=4.4). To be concluded, the pharmacokinetic study revealed that aspasomes formulation successively enhanced the bioavailability of TZN compared to oral drug. In conclusion, aspasomes could serve as an effective transdermal delivery of tizanidine hydrochloride.

Biography

Hadeer A. El-Hashemy, a specialized researcher at National Research Centre, Egypt. Technical committee member, UNESCO Egyptian National commission. Rapporteur of natural sciences and technology committee, UNESCO Egyptian national commission. Hold MSc degree in pharmaceutics & industrial pharmacy (2015). Hold PhD in pharmaceutics & industrial pharmacy from Cairo University (2019). Has an expertise in drug formulation and designing using nano technology. Filed of interest, is drug related problems and inventing novel formulations techniques and approaches like the usage of experimental design programs for tailoring and improving drug bioavailability and efficacy using nanotechnology in drug design and formulation.

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Fever is not a symptom in covid-19: None of the diseases require fever as its symptom

K. M. Yacob
Marma Health Centre, India

We have been hearing for centuries that 'fever is not a disease but a symptom'. Physicians say that fever is a symptom of diseases like flu to cancer.

The conservative fever definition, diagnosis, and treatments are based on fever as a symptom.

All the studies related to fever as a symptom of a disease have been done without knowing the Purpose of the temperature of fever is.

Without knowing the Purpose of the temperature of fever, how can fever included in the symptom definition?

Temperature between 38o to 41o centigrade can be symptom of a disease?

Most of the diseases may not have a fever. Sometimes it disappears. Then, is fever a symptom of which disease?

Symptom Definition is the only parameter necessary for a Symptom. As with any or all other definitions, symptom definition should describe the symptom scientifically. If it cannot describe clearly, there is no use of a symptom definition. A symptom is a departure from normal function or feeling which is noticed only by a patient, indicating the presence of disease or abnormality. One cannot be understood directly the temperature is elevated in the hypothalamus. A mechanical device is necessary to measure elevated temperature in the hypothalamus. In symptom definition, fever definition can't be found. The elevation of body temperature is not included in symptom definition.

Different cause of diseases never shows the same symptoms.

Different causes of diseases like virus, bacteria, fungi, venom, horror scene, horror dream,... never shows the same symptoms. Its actions are different and sometimes opposite. No similarities can be seen between their actions.

Elevated temperature or increased temperature never make fever or symptoms of fever. It may create hyperthermia.

None of the diseases or causes of diseases require fever as its symptom.

If the mosquito bites its virus, bacteria, venom gets deposited in the body as a result according to nature and strength of Viruses, bacteria, venom symptoms like itching, pain, and signals like colour change, inflammation may occur.

we can see the symptoms, Signals, and indications of the virus, bacteria, the venom which multiple or spreading or damages(disease) the body before fever

emerge. Patients who have flu to cancer may not have a fever.

How can we separate symptoms of the disease and symptoms of fever and symptoms of rising temperatures?

In fever, both symptoms of disease and symptoms of Fever are included. Deduct symptom of disease from total symptoms, we will get symptoms of fever.

(Disease +Fever)- Disease =Fever.

(Symptoms of disease +Symptoms of Fever)- Symptoms of disease =Symptoms of Fever (bitter taste, body pain, fatigue to mind and body, reduced appetite, reduced motion and indigestion, internal and external discomfort,…)

Like that we can separate signs, signals, and actions of both fever and disease.

(Signals of disease +Signals of Fever) - Signals of disease =Signals of Fever(high temperature, shivering, unconscious,....)

(Signs of disease +Signs of Fever) - Signs of disease =Signs of Fever.

(Actions of disease +Actions of Fever) - Actions of disease =Actions of Fever. In fever does not show any actions of temperature rise.

How can we prove the fever is not a symptom.

The fever is not symptom when examined in various directions. In fever, both symptoms of disease and symptoms of fever are included. Deduct symptom of disease from total symptoms, we will get symptoms of fever. we can separate signs, signals, and actions of both fever and disease and rising temperature.

Temperature between 38 degrees and 41 degrees cannot be a symptom of any of the diseases.

A different cause of diseases like virus, bacteria, fungi, venom, horror scene, and horror dream never shows the same symptoms.

Fever has never been scientifically proved as a symptom of a disease. Fever has the properties of adaptation.

If we ask any type of question-related to fever by assuming that the fever is not a symptom we will get a clear answer. If we avoid or evade from this we will never get a proper answer to even a single question.

Biography

K. M. Yacob is a practicing physician in the field of healthcare in the state of Kerala in India for the last 30 years and very much interested in basic research. My interest is spread across the fever, inflammation and back pain. I am a writer. I already printed and published nine books on these subjects. I wrote hundreds of articles in various magazines. After scientific studies, we have developed 8000 affirmative cross checking questions. It can explain all queries related to fever.

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Identification of generalized peptide vaccine candidates for SARS-COV-2 through computational analysis

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[2]Department of Electrical Engineering, Jadavpur University, India

[3]Computer Science Department, Government College of Engineering and Textile Technology, India

[4]Centre for Interdisciplinary Research and Education, India

Objective: The objective of this work is to identify common peptide vaccine candidates which are effective for all of the viral strains irrespective of frequent mutation of the invading pathogens.

Scope: Worldwide pandemic due to Coronavirus disease 2019 has been created an extreme crisis across the globe. Developing suitable vaccine is the ultimate solution to combat the crisis. As the virus mutates frequently, it is necessary to design a generalized vaccine candidates, which would be effective for all possible mutated strains. The protocol may be employed for any new invading pathogen.

Method: Firstly, using 2D Polar plot and Quotient Radius □(q□_R) characterization descriptor, we have identified all currently available mutated strains of SARS-CoV-2. Considering the frequency of occurrence, the top eight mutation strains have been chosen to identify suitable peptide regions for vaccine design. For identification of suitable regions, we have given emphasis on the surface exposed regions of the virus by studying Average Solvent Accessibility (ASA) profile and conserved region of the virus by using protein variability (pv) profile and then we have employed a mathematical – 2D Polygon Representation model. Further, we have checked the epitope potential using IEDB-AR and ensured that there is no case of any autoimmune threat by employing BLAST analysis. Finally, we have listed the suitable regions which are common for all mutated strains and could be used for developing vaccine.

Results: We have suggested generalized peptide regions which are potential peptide vaccine candidates against SARS-CoV-2 irrespective of not only its existing predominant strains but also of any possible variant in future.

Conclusion: Therefore, this new approach would be helpful to develop potential vaccine candidates against SARS-CoV-2 irrespective of any mutated form of this virus. This approach is also effective to design peptide vaccines against any other virus at present and in future.

Biography

Smarajit Manna, presently the Student Advisor, Jagadis Bose National Science Talent Search, Kolkata, India, did his B.Sc and M.Sc in Physics. He conducted his research work as at Jadavpur University, Kolkata and Delhi University South Campus, Delhi respectively in the field of Biophysics and subsequently received his Ph.D. degree from Jadavpur University. His research interests include statistical analysis and mathematical modelling of dynamical systems, Material Science and Bio-informatics. Currently, he has been working on mathematical modelling for peptide vaccine designing of newly emerging viruses. In his academic career, Dr. Manna has several research publications in national and international journals and acted as a co-author of book chapters.

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The role of synthetic and biological test systems in the development of transdermal drug delivery systems

E. G. Kuznetsova, O. M. Kuryleva, L. A. Salomatina and V. I. Sevastianov

The Shumakov National Medical Research Center of Transplantology and Artificial Organs, Ministry of Health of the Russian Federation, Russia

There are several approaches to modeling percutaneous diffusion of drugs. This work substantiates the combined use of synthetic and biological test systems at the initial stages of the Transdermal Drug Delivery Systems (TDDS) development using the synthetic low-molecular-weight compound Galavit® (aminodihydrophtalazinedione sodium) belongs to the class of immunomodulators as an example.

We investigated the release of Galavit® from emulsion TDDS of six different compositions through the synthetic test system represented by the Strat-M membrane (Merck Millipore) over 24 h of application (Table 1). Each TDDS contained 4.6 mg of Galavit®.

Table 1 shows that the amount of the drug that passed from Galavit® TDDS with compositions nos. 1 and 2 through the membrane into receiving chambers of the diffusion cells was about 30%.

Two compositions of emulsion TDDS were selected based on the results of screening tests, in which the largest amount of the medicine (30%) diffused into the receiving chamber of the Franz cell. The use of non-preserved rabbit skin revealed significant differences in this indicator for TDDS of these two compositions (Fig.1).

The mass of the drug that passed through the skin from the Galavit® TDDS over 24 h of

Weight of drug that passed through the membrane	Emulsion composition no.					
	1	2	3	4	5	6
%	29.8±7.1	31.0±5.6	19.0±4.0	8.0±2.1	14.0±3.7	20.0±5.2

Table 1. Quantitative Galavit® release from emulsion TDDS (n = 15) through the Strat-M membrane.

application was 58–71% for the first emulsion and 39–50% for the second.

The biological test system proved to be more sensitive to the emulsion compositions. Thus, the combined use of synthetic and biological test systems makes it possible to significantly reduce the complexity and costs of preclinical studies of the Galavit® TDS.

Pharmacokinetic studies of the Galavit® TDDS with the best emulsion composition have been carried out.

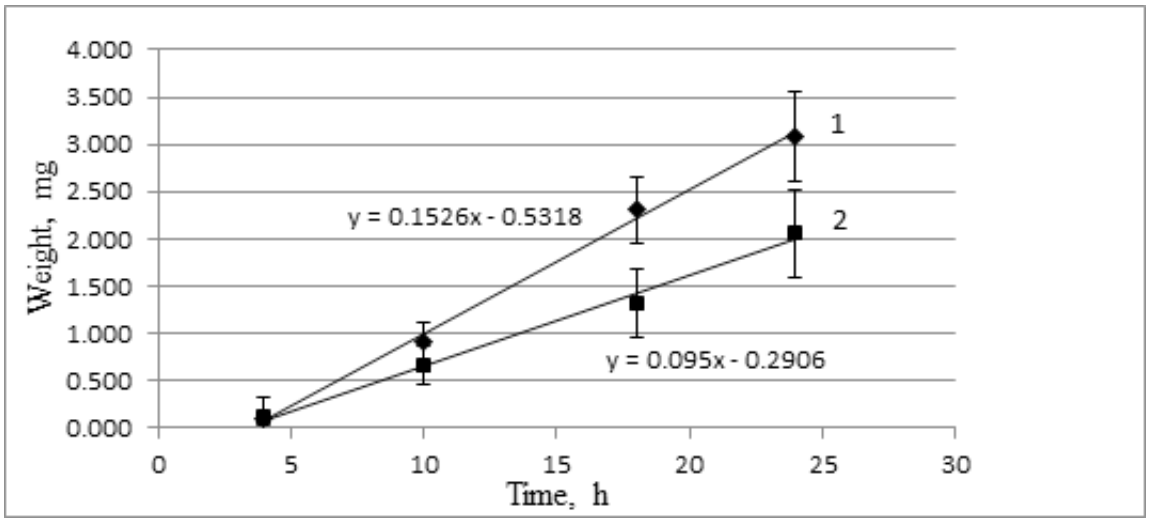

Fig. 1. In vitro diffusion of drug Galavit® through nonpreserved rabbit skin.

Biography

E. G. Kuznetsova works at Shumakov Federal Research Center of Transplantology and Artificial Organs, Ministry of Health of the Russian Federation since 2002, as a leading researcher since 2021.

She graduated at the Moscow Institute of Physics and Technology in 2002 with a degree in applied physics and mathematics. She studied at the correspondence postgraduate course of the Moscow Institute of Physics and Technology from 2002 to 2005. She defended her thesis "Development and research of transdermal insulin delivery systems" for the degree of candidate of biological sciences in the specialty "transplantology and artificial organs" in 2005.

The main scientific direction of Kuznetsova E. is the development and research of transdermal delivery systems for various drugs.

She mastered modern theoretical and experimental research methods during the work. She has 35 printed works.

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Cell penetrating sequential oligopeptide carrier: A multivalent molecule for intracellular targeting and biomedical applications

E. Fotou, Vasiliki Moulasioti, Vassilios Moussis and **Vassilios Tsikaris**

Department of Chemistry, University of Ioannina, Greece

The new era of biochemistry demands reliable substances that meet appropriate specifications for pharmaceutical use or diagnostic applications. That means biomolecules with high activity, low-cost, easy, and quick production, as well as respect for the environment. Peptides are very promising molecules in this direction, and they are widely used for such purposes.

This work aims to present a multivalent/ multirole "Cell Penetrating Sequential Oligopeptide Carrier (CPSOC)". CPSOC consists of the repetitive -Lys-Aib-Cys- moiety. Its design was based on the previously synthesized sequence (-Lys-Aib-Gly-), but CPSOC provided an effortless conjugation of the bioactive molecules. Lys holds a positively charged side chain that could interact with the cell membrane surface and contribute to the cell penetration, but much more aid to the solubility of the whole construct. Aib induces a helicoid conformation to the peptide backbone and protects from enzymatic degradation. Cys residue was chosen for linking biomolecules via stable thioether bonds.

CPSOC has advantageous properties as it can bind multiple copies of a bio-cargo; holds a determined 3D structure, constant after the conjugation with other molecules; does not alter the bio-cargo functionality; resists enzymatic degradation; is synthesized easily.

CPSOC has been proven an efficient molecule in 1) intracellular delivery of peptides derived from Cdc-42 protein for the inhibition of von Willebrand factor exocytosis; paclitaxel for antiproliferation activity in cancer cells; peptides derived from integrin αIIbβ3 for antiplatelet activity, 2) presenting antigenic peptides for antibodies production and diagnostic assays.

All these facts make CPSOC a promising tool for use in pharmaceutical/diagnostic applications, including 1) drug delivery for intracellular targeting and targeting of specialized cells that overexpress a specific molecule (e.g., cancer cells), 2) antigen delivery and recognition from antigen-presenting cells for immune response and consequently antibodies production, 3) antigen presentation for diagnostic/biological applications like ELISA.

Biography

Evgenia Fotou is a MSc, PhD Candidate in Department of Chemistry at University of Ioannina (Ioannina, Greece). She graduated from the Department of Chemistry at the University of Ioannina (2013). She obtained a master's degree in "Chemical and Biochemical Technologies" (2015) in the Laboratory of Protein and Peptide Chemistry, Department of Chemistry, University of Ioannina (Ioannina, Greece). She gained strong laboratory experience through Erasmus+ Placement Training in the Laboratory of Macromolecular Physical Chemistry, National Centre of Scientific Research, University of Lorraine (Nancy, France). She has attended several international/national conferences and presented many studies (oral and posters). She has participated in publications in international journals and as a reviewer in the "Journal of the Hellenic Veterinary Medical Society". Also, she participated in a pilot research program financed by the Agricultural Poultry Cooperative PINDOS (2017), while now she participates in two research programs (1. RESEARCH–CREATE–INNOVATE, EPAnEK 2014-2020 (T1EDK-03939); 2. ROP Epirus 2014-2020 (ΗΠ1ΑΒ-00178).

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The importance of doctor-patient relationship regarding medical malpractice claims

Anna Wszołek
Faculty of Law and Administration, Jagiellonian University, Poland

The relationship between doctors and patients has changed significantly over the last fifty years. Since the dawn of time, they have been based on the principle of paternalistic care, in which the stronger party with medical expertise extends care to the weaker party in the relationship. The patient, on the other hand, respected the doctor's recommendations and submitted to the therapeutic decisions made by him. The events of the Second World War, the dizzying progress of medicine and the conduct of scientific research on human beings without adequate information have led to stronger protection of human and patient rights. Recognition of the importance of individual autonomy caused transformation of the doctor-patient relationship into a more partnership or even consumer model.

Today, patients are much more aware of their rights and make more use of the means to protect them. The number of lawsuits for medical malpractice is also increasing, unfortunately not always those claims are justified. This paper presents, on the example of Poland, observations on how changes in the relationship between doctor and patient may have affected the decline in authority and trust in doctors and their perception in society, thereby fuelling an increase in claims against doctors and health care providers. The research is based on the comparison of the results of public opinion surveys between 1995 and 2021, statistics of medical malpractice cases, interviews and doctrine study.

Presented topic is a part of a scientific project entitled 'Legal protection of the reputation of a doctor as a party to unjustified medical malpractice proceedings', financed by the Ministry of Science and Higher Education of Poland within the "Diamond Grant" Programme. The study is of a primary research nature and merely signals certain problems for further analysis and development in-depth research.

Biography

Anna Wszołek ia a PhD candidate at the faculty of Law and Administration of the Jagiellonian University, Kraków, Poland and a solicitor trainee. Graduated from Jagiellonian University in 2017 with a bachelor's degree in intellectual property law and new media, and in 2019 with a master's degree in law. Between 2019 and 2020 a trainee of Pan-European Seal Programme in European Patent Office in Munich. Laureate of the Scholarship of the Minister and Science of Higher Education of Poland (2017). Laureate of the VII edition of 'Diamond Grant', a program of the Ministry of Science and Higher Education of Poland which finances research of young scientists and enables them to start a doctoral dissertation before completing a master's degree (2018).

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Prostate cancer and cholesterol metabolism

M. Ulamec

Scientific Group for Research on Epigenetic Biomarkers, University of Zagreb, Croatia

Prostate cancer is one of the two most common malignant tumors of the men. Disturbed lipid metabolism and abnormal cholesterol accumulation is important in the pathogenesis of the disease. Cholesterol homeostasis in the cell is balanced by SREBP2 and LXR activity, which is related to endoplasmic reticulum cholesterol level. Many dysregulated pathways in PC are implicated in SREBP2 activation which can influence increased membrane/ lipid rafts synthesis and protein prenylation alter membrane composition and cell signaling. Cholesterol serves as precursor for intracellular androgen synthesis and SREBP2 supports tumor growth by providing cholesterol as building block for membrane synthesis, lipid rafts and androgen synthesis, while via mevalonate pathway provides molecules required for molecular membrane docking and modification, ferroptosis inhibition, energy, and nucleotide production. Commonly dysregulated signaling pathways in PC (PI3K/AKT/MTOR, MAPK, AR and p53) are related to cholesterol homeostasis regulation as well.

Comprehensive analysis that would encompass genomic, transcriptomic, and proteomic data considering tissue homogeneity are required as well as stratification of patients according to stage, Gleason score, interindividual genetic diversity and adjuvant treatments would pave the way for personalized approach and long-term treatments.

Biography

Monika Ulamec is a Surgical Pathologist with a main interest in the uropathology, pediatric pathology, molecular pathology; Assistant professor of Pathology, Scientific associate at the School of Medicine, University of Zagreb. She is a Reviewer at the Scientific J (Journal of Health Sciences, Case Reports in Pathology, Cancer Cell International, Virchows Archive). She has publications of 62 papers according Medline (February 2022); more than 820 citations according Web of Science (February 2022); H index 40 (February 2022).

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Identification of specific Bromodomain family members as potential therapeutic targets in stem cell-like tumors

P. Czerwinska[1,2], A.M. Jaworska[1], N.A. Wlodarczyk[1] and **AA. Mackiewicz[1,2]**

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[2]Department of Diagnostics and Cancer Immunology, Greater Poland Cancer Centre, Poland

Cancer de-differentiation, which entails the acquisition of stem cell-like molecular features, is mediated by the transcriptional and epigenetic aberrations in cancer cells. The stem cell-like compartment of the primary tumors exhibits higher metastatic potential and facilitates tumor relapse after treatment due to intrinsic resistance to standard therapies. Therefore, there is a great need for novel drugs directly eradicating cancer stem cell-like cells.

Recently, Bromodomain (BrD) proteins have emerged as potent therapeutic targets, with several promising inhibitors already in the clinical evaluation. BrD proteins – a family of about 40 epigenetic factors – are involved in the pathogenesis of several tumor types, although their association with cancer stemness remains largely unknown.

Here, we have harnessed The Cancer Genome Atlas (TCGA) and the Gene Expression Omnibus (GEO) data for 27 distinct solid tumor types and used several bioinformatic tools (i.e., Oncomine, PrognoScan, GEPIA2, TIMER2.0, TISIDB, GSEA, R2 platform) to characterize the association between the BrD family members and cancer stemness and to identify the most promising targets for stem cell-like tumors.

Our approach identified two potential members, namely ATAD2 and TRIM28, consistently associated with an enriched cancer stem cell-like phenotype. ATAD2 and TRIM28 are significantly overexpressed in higher-grade tumors that manifest stem cell-like molecular traits. In contrast to most BrD members, the transcriptome profiles of high TRIM28 or high ATAD2 expressing tumors are robustly enriched with stemness markers and targets for c-Myc transcription factor. The in vitro 3D models further confirmed a fundamental role for TRIM28 in regulating cancer stemness, as TRIM28 knockdown significantly inhibited sphere formation.

Our results demonstrate for the first time the correlation between distinct BrD family members and cancer de-differentiation status, highlighting the versatility of ATAD2 and TRIM28 association with cancer stemness and suggesting ATAD2 and TRIM28 as novel druggable targets for de-differentiated tumors.

Biography

Patrycja Czerwińska is a young scientist currently working at the Department of Cancer Immunology, Poznań University of Medical Sciences. She completed her Ph.D. at Medical University of Warsaw and her undergraduate studies at Poznań University of Medical Sciences. Her research focuses on characterizing the molecular mechanisms that facilitate cancer stem cell-like phenotype acquisition to identify novel therapeutic targets. Her work also aims to delineate the anti-tumor immune responses against stem cell-like cancer cells to improve the efficacy of current therapeutic strategies. She has been published extensively as author and co-author of 18 papers in highly regarded, peer-reviewed journals. The promoter of several bachelor and engineering theses. Chairman of the Undergraduate Research Club at Poznań University of Medical Sciences, improving skills in bioinformatics.

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Preventing COVID-19 through Indian spices

Amit Jaiswal[1], Pradeep Yadav[2] and Rajiv Kumar Singh[2]

[1]Faculty of Biological Sciences, Friedrich Schiller University, Germany
[2]Faculty of Life Science, Rajiv Gandhi University, India

Corona Virus Disease (COVID-19) has claimed over 4.1 million human life across the globe which is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Scientists all over the world are in search of various molecules to get a potential anti-COVID-19 drug. Spices contain certain phytochemicals which possess antiviral, anti-bacterial, and anti-fungal properties. Therefore, in order to search such potent drug, we studied first screened few popular plants and then selected eighteen well reported antiviral phytochemicals from some commonly used spices in Indian tradition viz. Curcuma longa (Turmeric), Nigella sativa (Black cumin) and Trachyspermum ammi (Carom) to know whether they can avert SARS-CoV-2 infection. At first, we predicted the structure of TMPRSS2 (transmembrane protease serine 2), a host protein that facilitates the entry of spike protein of SARS-CoV-2 through endocytosis. We then performed molecular docking against its catalytic domain with the previously screened phytochemicals as well as a known inhibitor of TMPRSS2 – Camostat. We then analyzed the stability of best docked phytochemicals along with camostat by using Molecular Dynamic Simulation (MDS). Simulation studies indicated carvacrol and thymol as better inhibitors in comparison to camostat due to their stable binding with TMPRSS2 in its catalytic domain which comprises of an oxyanion hole having catalytic triad residues. Further these phytochemicals are naturally abundant and possesses least side-effects and therefore carvacrol and thymol could serve as a wonder molecule against COVID-19 and could be an efficient alternative to current vaccines.

Biography

Amit Jaiswal (PhD) is a graduate student at the University of Jena, Germany. He received his M.Sc. degree in Biotechnology from Bangalore University and B.Sc. in Life Sciences from Dibrugarh University. His research lies in the interface of Bioinformatics and Stem Cell Biology. He aims to understand the molecular interactions within the cells which can influence their cell fate and whether these fates could be altered.

Emulsion adjuvants in vaccines stepping up to meeting the pandemic challenge

Rushit Lodaya

GSK – Rockville Center for Vaccines Research, USA

Emulsion adjuvants have been licensed for seasonal and pandemic use with influenza vaccine and used for more than two decades. Particularly squalene based emulsions MF59 and AS03 have been used with over 100 million doses administered in humans demonstrating safety. Substantial clinical experience of effectiveness, a well-established safety profile, along with the ease of manufacturing have established emulsion adjuvants as one of the leading platforms for the development of pandemic vaccines. These adjuvants allow for antigen dose sparing, more rapid immune responses, and enhanced quality and quantity of adaptive immune responses. Emulsion adjuvants show robust Th1/Th2 T cell response by typically creating an immunocompetent environment at the site of injection causing enhancing immune cell recruitment. Hence these adjuvants were used in 2009 H1N1 pandemic and are currently being evaluated in three independent phase III studies for the SARS CoV2 pandemic.

Although these emulsions can be manufactured in a GMP facility and millions of doses have been produced; newer and simpler methods of manufacturing may be needed particularly to meet the global supply at the time of a pandemic. Additionally, evident from the current use of GLA-SE and SLA-SE (emulsion adjuvants from Infectious Diseases Research Institute - IDRI) in clinical development, emulsions can be explored further as a delivery platform for immune potentiators. Tapping the wealth of knowledge on nanoemulsions as pharmaceutical delivery method, novel emulsion adjuvants can be formulated and optimized to deliver immune potentiator(s) and improve the breadth of immune response.

In summary, the history of use of emulsion adjuvants offer abundant key learnings that can be built upon to discover novel and next generation emulsion adjuvants. This presentation will comprehensively review emulsion adjuvants, its mechanism of action, as well as emerging novel methods to manufacture these adjuvants. It will also discuss pharmaceutical properties of emulsions that can be manipulated for optimized delivery of immune potentiators.

Biography

Rushit Lodaya done his PhD in Pharmaceutical Sciences at Northeastern University, Boston, MA June 2019 and completed his Master of Science in the year May 2013. He completed his Bachelor of Science in Pharmacy at Mumbai University, Maharashtra, India May 2010. He is Subject Matter Expert in vaccine adjuvant formulation and characterization, Proficient in nanoparticle formulation development for nucleic acid delivery, Competent with preparation, characterization and stabilization of small molecule nanoparticle suspensions for oral and parenteral delivery. He has Experience with solid state characterization, salt-screening and other pre-formulation activities to enhance physicochemical properties of small molecule compounds, Adept in writing protocols and technical reports to aid commercial scale batch production. He has Experience in designing research projects for interns and PhD students and supervising the execution.

KEYNOTE PRESENTATIONS

DAY 2

PEERS ALLEY MEDIA

Virtual Event

International Conference and Exhibition on

The Future of Pharmaceutics and Novel Drug Delivery Systems

March 28-29, 2022

FUTURE PHARMA 2022

BIOGRAPHY

Jack Ray Gallagher, founder and chief scientist, Clarity Pharma Research LLC, is an internationally recognized medical/health care researcher/conference presenter, an editor of *Current Trends in Clinical and Medical Sciences,* expert reviewer for *Journal of Chemotherapy,* and former director of a multi-university research consortium (University of Virginia School of Medicine). He has authored more than 130 scientific publications including a first-place paper on future challenges presented at the Second International Conference on Marketing and Development in Budapest. The interview by OncLive about his real-world research presentation on side effects of PARP inhibitors at the European Society for Medical Oncology Congress 2018 (Munich) was selected for distribution to oncologists worldwide and published in *Future Oncology* (Dec. 2019). He co-chaired the gynecological oncology sessions at PCS 4th Global Obstetrics & Gynaecology 2019 Congress (Prague). He is a mathematician, doctorate-level clinical psychologist, epidemiologist, former decathlete, and inventor of a remote-control guidance system for blind athletes.

Jack Ray Gallagher

Founder and Chief Scientist, Clarity Pharma Research LLC, USA

New methodologies for population-based rare disease epidemiology: Cost-Effective/multi-country examples

Objectives and Scope: Rare disease estimates worldwide range from 6,000 to 7,000, affecting possibly 300 to 400 million persons. The rare-disease treatment market is widely expected to experience explosive growth during the foreseeable future as is evidenced by the rapidly increasing number of clinical-stage start-up pharmaceutical companies focused on drug-discovery for one or more rare conditions. Thus, the rare-disease segment is extremely important to the pharmaceutical industry.

The most basic question a pharmaceutical company must answer to develop an effective strategic plan for one of these diseases is "how many potential patients in our target area need an effective treatment (expected market size)?" Unfortunately, accurate and reliable answers to this question almost always require a company to sponsor the necessary epidemiological research. This can be particularly burdensome for clinical-stage start-up companies.

The purpose of this presentation is to share new, highly successful, nationally representative, and cost-effective methodologies for rare-disease treatment prevalence studies.

Conclusion: This study shows that new or enhanced methodologies can be employed to provide confidence-building target-patient prevalence estimates to stakeholders, including investors and potential investors. This was particularly important for the company noted here because its initial estimates of NTM-PD prevalence in the United States, which were based on insurance claims data, greatly underestimated the size of this market and in turn inhibited investor enthusiasm. Our researchers designed and implemented a physician/patient chart observational study that corrected for the 30% of NTM-PD claims in the national database that we found were misclassified or unclassified,

thus substantially increasing the estimated size of the NTM-PD market in the U.S.

The multi-country study provided the pharmaceutical company with important estimates of NTM-PD prevalence at the regional level for each country, insights not possible with other population-based methods because of the cost-prohibitive corresponding regional study sample sizes needed.

SCIENTIFIC ABSTRACTS

DAY 2

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Novel voltage gated calcium channel blocker inhibits the proliferation of oral squamous cell carcinoma

R. Chakraborty[1], C. Darido[2], H. Hu[1] and **K. Vickery[1]**

[1]Macquarie University, Australia

[2]Peter MacCallum Cancer Centre, Australia

Introduction: Oral squamous cell carcinoma is one of the most prevalent cancers worldwide, resulting in high morbidity and mortality rates. Calcium channels are linked directly or indirectly to all the 'hallmarks of cancer. Perturbation of calcium signaling occurs due to the pronounced changes in (a) expression levels, (b) altered cellular localization, (c) altered post-translational modifications, and (d) genetic mutations. ML218 HCl as a T-type voltage-gated calcium channel [Cav 3.2 and Cav 3.3] inhibitor. We hypothesized that ML218 HCl could be effective in reducing oral cancer cell proliferation.

Objectives: Determine (a) the metabolic and viability effect of ML218 HCl on oral cancer cell proliferation, (b) the effect of ML218 HCl on oral cancer cell apoptosis, (c) the effect of ML218 HCl on proliferation factors.

Methods: Oral cancer cells Cal 27, SCC25, SCC9, SCC4, and normal oral cell OKF6 used during the project. The maximum amount of ML218 HCl tested against oral cancer cells was 100 µM. Real-time Glo MT and Trypan Blue assay used to determine metabolic effect and cell viability respectively. Western Blot and ELISA was used to determine the relative protein expression of proliferation pathways related proteins.

Results: ML218 HCl inhibited oral cancer cell proliferation, increased apoptosis and cell death. ML218 HCl reduced metabolism and viability of oral cancer cells by 100% and 70% respectively, after 24 h drug treatment. Treatment with ML218 HCl reduced TNFα production significantly ($p \leq 0.0001$).

Conclusion: ML218 HCl surely inhibits oral cancer cell proliferation. Voltage gated calcium channel drugs should be considered for future head and neck research.

Biography

Rajdeep Chakraborty is a Head and Neck Cancer Researcher at Macquarie University (MQ), Sydney. He is a trained Dentoalveolar surgeon who did his master's in biomedical sciences from Lancaster University, U.K and later completed his Master of Research in oral cancer at MQ after achieving the prestigious MQ Research Excellence Scholarship and Sydney Vital Translational Cancer Research Scholar Award. He initiated oral cancer research at Macquarie University after collaborating with Peter MacCallum Cancer Research Centre, Melbourne University and Diamantina Research Institute, Head and Neck Cancer Research Centre, University of Queensland. Due to his academic and professional achievements he was appointed as Early Career Researcher Symposium Organizing Committee member by Sydney Vital. He is also a member of several international cancer associations. He is one of the rare academicians who combines dental surgery practice and fundamental science research.

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A systematic review of literature of *In vitro* and *in vivo* antiplasmodial, antimalarial activities of African medicinal plants

Faham Khamesipour[1,2] and **Saeed Nezaratizade**[2]

[1]*Shahid Beheshti University of Medical Sciences, Iran*

[2]*Shahrekord Branch, Islamic Azad University, Iran*

Background: Malaria still constitutes a major public health menace, especially in tropical and subtropical countries. Close to half a million people mainly children in Africa, die every year from the disease. With the rising resistance to frontline drugs (artemisinin-based combinations), there is a need to accelerate the discovery and development of newer anti-malarial drugs. A systematic review was conducted to identify the African medicinal plants with significant antiplasmodial and/or anti-malarial activity, as wells as assessing the variation in their activity between study designs (in vitro and in vivo).

Methods: Key health-related databases including Google Scholar, PubMed, PubMed Central, and Science Direct were searched for relevant literature on the antiplasmodial and anti-malarial activities of African medicinal plants.

Results: A majority of research articles were studies conducted in Nigeria. In all, there were 722 independent studies. A 40 (5.5%) were both in vitro and in vivo. For studies reporting both the in vitro and in vivo activity, a majority of 17 (42.5%) reported only moderate activity, 13 (32.5%) studies reported very good activity and 10 (25.0%) reported good activity. Among the plants with very good activity, only one species demonstrated very good activity both in vitro and in vivo (Table 3).

Conclusions: Although there are many indigenous plants with considerable antiplasmodial and anti-malarial activity, the progress in the development of new anti-malarial drugs from African medicinal plants is still slothful, with only one clinical trial with Cochlospermum planchonii (Bixaceae) conducted to date. There is, therefore, the need to scale up anti-malarial drug discovery in the African region.

Biography

Faham Khamesipour currently works and researches at some Iranian research center, and University. He does research in veterinary medicine, parasitology, health policy, medical education, zoonoses disease and traditional medicine. He is an author of seven books and more than 110 peer-reviewed papers in the fields of microbiology, parasitology, zoonoses, herbal medicine, molecular study, infection disease, and pathology. Received over 16 awards. He also an editor of many national and international journals and reviewer for some international journals. He participated in 11 workshops and training courses, and 25 conferences. He is a member in many associations. He is also the head and scientific secretary of the first National Congress on Zoonoses in Iran. He is a high achiever, competent in his field, enthusiastic, and an elite member of the research/teaching community in Iran in the fields of parasitology, infectious diseases and zoonotic, herbal medicines, food science, and veterinary biology, He is recognized by his government to be a leader in his field and has received many awards, scholarships, and other accolades. He is proactive and ambitious and makes major contributions to the research and teaching environment.

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Understanding transcriptomics of neurodevelopmental disorders: A computational approach

Prachi Srivastava and **Prekshi Garg**

Amity Institute of Biotechnology, Amity University, India

The human brain is one of the most complexed organs of the body with complicated biological system, cell types, neural circuits, functionally distinct regions and approximately ten thousand genes expressed in each region. Brain development is dependent on the expression of gene products, RNA and protein. Mutations in these gene products result in altered gene function and structure that consecutively gives rise to neurodevelopmental disorders. Neuro Developmental Disorders (NDD) are multi-factorial disorders that depict impaired cognition, communication, behavior and motor skills ultimately leading to abnormal brain development. Whole exome or transcriptome analysis has helped in increasing our understanding of mechanisms related to NDD, development of precise medicine and targeted treatment. Transcriptomics study has made identification of differentially expressed genes and key biological processes and pathways possible. This information has greatly benefitted neurodevelopmental research. The neurological diseases are now being studied and analyzed from transcriptomic perspective as well to get a better insight into the disease. The results from such studies are applied in designing gene therapy, personalized medicines and identification of biomarkers for that disease. Therefore, the transcriptomic studies have opened new doors to neurodevelopment research that can help in better understanding, diagnosis and treatment of neurodevelopmental disorders.

Biography

Prachi Srivastava was awarded her doctorate from Lucknow University in 2004. She has made significant research contributions in bioinformatics in different domains. She has presented papers in national and international forums & conferences; is recognized by journals of high repute as she has 75 publications and more than a hundred of her abstracts, many chaired sessions to her credit. In addition to presenting her research, she has actively organized many national and international conferences, seminars, training programs, and FDP and delivered invited talks and guest/keynote lectures at different national and international scientific forums and academic platforms. She was won many awards during her academic and scientific journey including STOX Gold Medal, AEB Best paper presentation award, BRPM award, Faculty appreciation award From DOEACC Lucknow center, 'Parashakti' award of Amity Lucknow Campus for Academic excellence. Recently, she was awarded the coveted international JNS Travel Award (Japan Neuroscience) and also conferred with 'Fellow of the National Academy of Environmental Biology (FNAEB)' along with Meritorious award of AEB. She was granted three copyrights 'GeVan, 'Tulna', and Pest i with her group in reference to her high throughput computational pipelines and tool. she is a member of many international societies & advisory boards, reviewer, and editorial team for numerous national and international journals of high repute. Her students mirror her passion and more than eighteen of her students have won different awards at the national and international level, under her mentorship. Furthermore, Eleven of her supervised students have been awarded a doctorate and are successfully working in their domains. Currently, she is mentoring four students for their doctoral research. Not only as an academician but as an honorary biotechnology counselor, she presents counseling seminars talking about a career in biotechnology and bioinformatics at different places.

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Hansen solubility theory in the extraction of policosanol from sugarcane wax

Eduardo Hernández Ramos and **M. De los Ríos**

Cuban Research Institute of Sugarcane Derivatives, Cuba

Policosanol has a recognized efficacy as a treatment for coronary heart disease and its effect as a neuroprotective is being studied in recent articles. Cuba is a pioneer in obtaining this drug from sugar cane; recovering it from a by-product of the sugar production process as part of a mixture of waxy substances. The extraction and refining process of sugar cane wax is based on solvent extraction. The objective of this research is to base changes that improve the sugar cane wax extraction and refining process for the production of policosanol in terms of efficiency, economy, environmental effects and compliance with product quality requirements. Hansen's theory explains in a practical way the affinity that is created between a solute and a solvent. By determining the Hansen solubility parameters, it is possible to analyze the affinity of the solute with different solvents using a tool such as Excel or the Hansen Solubility Practice Parameter Program (HSPiP). From the application of this theory, the solubility parameters that characterize the oil fraction present in the sugar cane wax and the refined wax were obtained. From these results, a criterion was created as to which solvent or solvent mixtures would be suitable for a more in-depth study of the solubility of the wax fractions in them. Independent analysis of the fractions concluded that absolute ethanol is suitable for the extraction of the oil fraction and toluene for the refined wax.

Biography

Eduardo Hernández Ramos is a young Cuban leader in the field of nutraceutical product extraction processes. He has participated as a speaker at national and international events in his country. He has been published by peer-reviewed journals indexed on the web of science and Scopus as author and co-author. He works as a researcher at the Cuban Research Institute of Sugarcane Derivatives, participating in innovative projects related to the extraction and refining of sugar cane wax as a raw material for obtaining policosanol. He is a student of the doctoral program at the José Antonio Hecheverría Technological University of Havana (CUJAE) "Sciences of the Engineering of Chemical, Biotechnological and Food Processes".

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The neuroprotective effect of artemisinin and its analogs and their implication in the treatment of ischemic stroke

Wenhua Zheng, Shuai Li, Chen Yi Tian, Xingan Xing, Wenshu Zhou, Chao Yang and Zhiwei Zhou

University of Macau, China

Ischemic stroke is one of the leading causes of death and disability among adults. Despite the economic burden of the disease, available treatment options are still very limited. With the exception of anti-thrombolytics and hypothermia, current therapies fail to reduce neuronal injury, neurological deficits and mortality rates, suggesting that the development of novel and more effective therapies against ischemic stroke is urgent. In the present study, we found that artemether, which has been used in the clinic as an anti-malarial drug, was able to improve the neurological deficits, attenuate the infarction volume and the brain water content in a middle cerebral artery occlusion (MCAO) animal model. Furthermore, artemether treatment significantly suppressed cell apoptosis, stimulated cell proliferation and promoted the phosphorylation of extracellular signal-regulated kinase 1/2 (ERK1/2), P90rsk and cAMP responsive element-binding protein (CREB). Artemether protective effect was attenuated by PD98059, an ERK1/2 inhibitor, administration. Similarly, in an in vitro oxygen-glucose deprivation/reperfusion (OGD/RP) model, artemether pre-treatment induced the suppression of the intracellular ROS, the down-regulation of LDH activity, the reduction of caspase 3 activity and of the apoptosis cell rate and reversed the decrease of mitochondrial membrane potential. As with MCAO animal model, artemether promoted the activation of Erk1/2-P90rsk-CREB signaling pathway. This effect was blocked by the inhibition or knock-down of ERK1/2. The present study provides evidences of the neuroprotective effect of artemether unravelling its potential as a new therapeutic candidate for the prevention and treatment of stroke. Supported by NFSC (31771128 and 31371088), MYRG2016-00052-FHS and MYRG2018-00134-FHS from the University of Macau, and the Science and Technology Development Fund (FDCT) of Macao (016/2016/A1 and 0113/2018/A3). *Corresponding Author

Biography

Wenhua Zheng, Professor, Principle Investigator in Faculty of Health Science, University of Macau, leading a group of scientists working on aging and neuronal degenerative disorders. He is a Section Editor for Encyclopedia of Gerontology and Population Aging; a Lead Guest Editor and Editor for several journals. Grant Reviewer for NSFC, Poland and CIHR in Canada. He is an Honorary Professor at the University of Queensland (QS45) and an Adjunct Professor/visiting Prof at RMIT University and other universities. Dr Zheng has published >150 papers which have been cited over 6500 times.

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Does fever increase or decrease blood circulation?

K. M. Yacob
Marma Health Centre, India

This is the first time many people have heard such a question.

When it comes to treating back pain, neck pain, and knee pain, it is often heard that the cause of the pain is reduced blood flow. A variety of heat-inducing devices are used to increase blood flow to the lower back, neck, and knee pains. Physiotherapy often provides more heat than fever.

To this day, no one has heard that fever is caused by poor blood flow.

As the disease progresses, blood flow decreases. Body tingling, body aches, and narrowing of the blood vessels under the skin are the signs, symptoms, and signals of decreased blood flow. Signs, symptoms, and signals of decreased blood flow show before the onset of fever.

When the disease becomes a threat to life or organs blood circulation decreases, Temperature of fever will emerge to increase prevailing blood circulation.

It is a well-known fact that as the disease progresses, blood flow decreases and this can lead to death. When there is a decrease in blood flow and its signs, symptoms, and signals, the immune system do actions to increase blood flow to save lives. It has been proven around the world that all types of heat increase blood flow. The heat of the fever increases the blood flow. Fever increases blood flow, which means more lymphocytes flow through lymphoid tissues. If the heat of the fever increases the blood flow, reducing the heat reduces the blood flow. It will increase inflammation and infection and finally, death will occur.

According to physics, it is foolish that when fever temperature is reduced, shows the symptoms, signs, and signals of reduced blood flow, are ignored and then treated to reduce the heat again. The fever is heat energy. To date, modern science has not studied what actions were carried out heat on fever.

The cause of all complications, including death, is the treatment of fever without knowing why it is hot.

What kind of treatment should be given if you have symptoms of decreased blood flow?

Treatment should be to increase blood flow.

This is the basic principle of physics.

Is there any benefit in reducing body heat during fever?

There is no merit of any kind.

Not only is it of no benefit, but it also causes death by inflammation and infection.

The actual treatment for fever is to increase blood circulation. Two ways to increase blood circulation. 1. Never allow body temperature to lose 2. Apply heat from outside to the body. When the temperature produced by the body due to fever and heat which we applied to the body combines together, the blood circulation increases.

Heat-reducing fever treatment with water and paracetamol should be banned as soon as possible.

Biography

K. M. Yacob is a practicing physician in the field of healthcare in the state of Kerala in India for the last 30 years and very much interested in basic research. My interest is spread across the fever, inflammation and back pain. I am a writer. I already printed and published nine books on these subjects. I wrote hundreds of articles in various magazines. After scientific studies, we have developed 8000 affirmative cross checking questions. It can explain all queries related to fever.

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Effects of replacing fishmeal with dietary dried distillers grains with solubles on growth, serum biochemical indices, antioxidative functions, and disease resistance for Litopenaeus vannamei juveniles

Gyan Watson Ray[1,2,3], Qi-hui Yang[1,2,3], Beiping Tan[1,2,3], Xiaohui Dong[1,2,3], Shuyan Chi[1,2,3], Hongyu Liu [1,2,3] and Shuang Zhang[1,2,3]

[1]College of Fisheries, Guangdong Ocean University, China

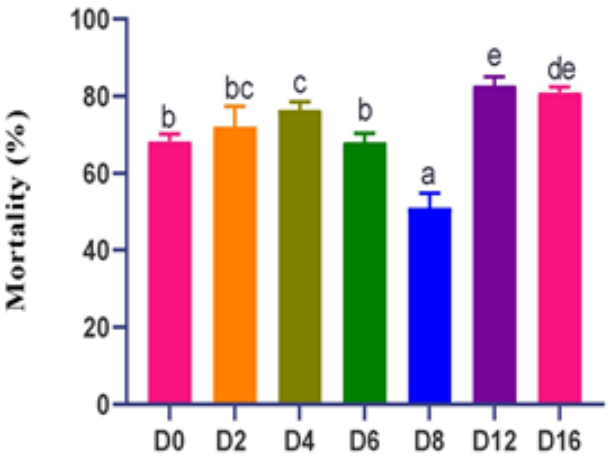
[2]Key Laboratory of Aquatic, Livestock and Poultry Feed Science and Technology in South China, China

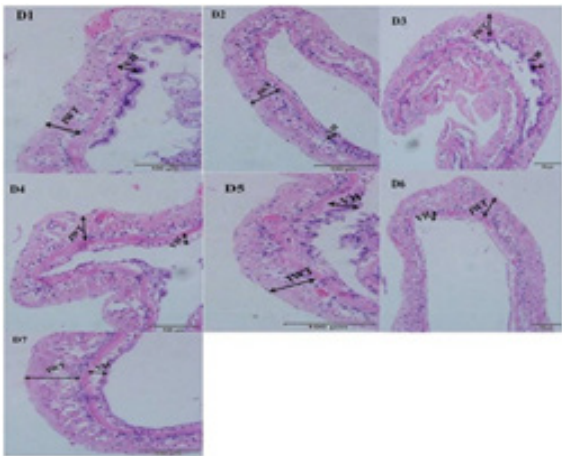
[3]Aquatic Animals Precision Nutrition and High-Efficiency Feed Engineering Research Center of Guangdong Province, China

This research was conducted to assess the effects of replacing fishmeal (FM) with Dried Distillers Grains with Solubles (DDGS) at various levels (D0 (0 %), D2 (2 %), D4 (4 %), D6 (6 %), D8 (8 %), D12 (12 %), and D16 (16 %)) on the growth, proximate body composition, serum biochemical indices, antioxidant activities, histology, and disease resistance in juvenile Pacific whiteleg shrimp. Forty shrimp per tank were stocked in seven different tanks with three replicates of each treatment group with an initial weight of 0.23 ± 0.00 g. Their respective experimental diets were used to feed shrimp for 56 days. The results showed an enhancement in shrimp fed dietary DDGS (D8) diets on the growth performance, including final weight, weight gain, acid phosphatase, alkaline phosphatase, glucose, and total antioxidant capacity in the serum ($P < 0.05$). Decreased FCR and HighDensity Lipoprotein Cholesterol were observed in shrimp fed DDGS (D8) diets in serum compared to D0. No severe changes and significant differences in villus height and intestinal wall thickness were observed in the shrimp hepatopancreas and mid-gut among treatment groups. Furthermore, disease resistance increased in shrimp fed the DDGS diet, with D8 obtaining the lowest mortality rate, 50.9 %, compared to the control group (D0), 68.3 %. In summary, regarding all the factors, replacing FM with DDGS at D8 (8 %) in the shrimp diet could modulate and cater to overall growth performance, health and immunity, histology, and disease resistance in shrimp. Table 1, below shows the feed formulation table used to feed the shrimp, figure 1, and 2 shows mortality rate after shrimp have been fed with experimental diets and challenged with bacteria, and lastly the histological analysis in shrimp intestine respectively.

Ingredients and nutritional composition of experimental diets (% dry matter).

Ingredients (%)	D0(0%)	D2(2%)	D4(4%)	D6(6%)	D8(8%)	D12(12 %)	D16(16 %)
Brown fishmeal[a]	20	18	16	14	12	8	4
DDGS[a]	0	2	4	6	8	12	16
Soybean meal[a]	15	15	15	15	15	15	15
Peanut meal[a]	12	12	12	12	12	12	12
Beer yeast[a]	6	6	6	6	6	6	6
Shrimp shell powder[a]	6	6	6	6	6	6	6
Flour[a]	23	23	23	23	23	23	23
Calcium dihydrogen phosphate[a]	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Vitamin C[a]	0.03	0.03	0.03	0.03	0.03	0.03	0.03
Choline[a]	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Lecithin[a]	1.5	1.5	1.5	1.5	1.5	1.5	1.5
FO&SBO(1:1)[a]	3	3	3	3	3	3	3
Mineral premix[b]	1	1	1	1	1	1	1
Vitamin premix[c]	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Lysine[a]	1	1	1	1	1	1	1
Methionine[a]	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Arginine[a]	0	0.03	0.05	0.08	0.11	0.17	0.22
Threonine[a]	0.09	0.11	0.13	0.15	0.16	0.21	0.24
Microcrystalline cellulose[a]	8.83	8.78	8.74	8.69	8.65	8.54	8.46
Proximate composition (%)							
Moisture[d]	9.95	10.39	10.56	10.55	10.65	10.72	11.04
Crude protein[d]	32.53	32.12	32.16	32.21	32.34	32.2	32.29
Crude lipid[d]	7.49	7.53	7.76	8.03	8.21	8.04	8.19
Ash[d]	8.35	8.71	8.77	8.66	8.76	9.17	10.71
NFE[e]	41.68	41.25	40.75	40.55	40.04	39.87	37.77
Gross energy (kJ g^{-1} diet)	16.8	16.9	16.7	16.6	16.4	16.5	16.6





Biography

Gyan Watson Ray is a dynamic and ambitious professional scientific researcher and author combining a strong academic background with valuable experience in fisheries and the aquaculture industry around the world. Possess excellent written skills and oral communication acquired from exposure to the academic and scientific environment and I'm adept at liaising with scientific researchers and stakeholders of the fisheries and aquaculture industry at various levels. I also thrive best in the autonomous and team-based role and display the initiatives, diligence, and drive required to excel under pressure. My objective is to keep learning and improve myself every day to bring out the best in me and help others. My vision is to learn new skills and to bring out new scientific knowledge to improve the fisheries and aquaculture industry in the world and use aquaculture as a tool to eliminate poverty in our society.

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Complex of breast milk antimicrobial peptides as a source of natural antibiotics

Tatiana Kolyganova[1,2] and **Vera Arzumanian**[1]

[1]*Department of Microbiology, Virology and Immunology, Mechnikov Research Institute for Vaccines and Sera, Russia*

[2]*Department of Microbiology, Virology and Immunology, Sechenov University, Russia*

Human breast milk contains a large number of immune factors, some of them are Anti-Microbial Peptides (AMP) - substances with pronounced antimicrobial activity, among which lactoferrin (LF), lysozyme (LC) and lactoperoxidase (LP) are the prevailing AMP.

Objects: Cell cultures of Candida albicans No. 927, Staphylococcus aureus Wood 46, and Escherichia coli M 17.

Methods: Activity was assessed using preparations of LF, and LP obtained from breast milk pools of healthy mothers (Lactobio, Moscow, Russia), and LC (AppliChem, USA). The assessment of antimicrobial activity was carried out by combining of the preparations with microorganism cell suspensions, incubation, sedimentation of cells and their treatment with the dye bromcresol purple, repeated incubation, and sedimentation of cells, followed by spectrophotometry of the supernatant.

Results: LF, LP and LC have a direct antimicrobial effect on the cells of the studied

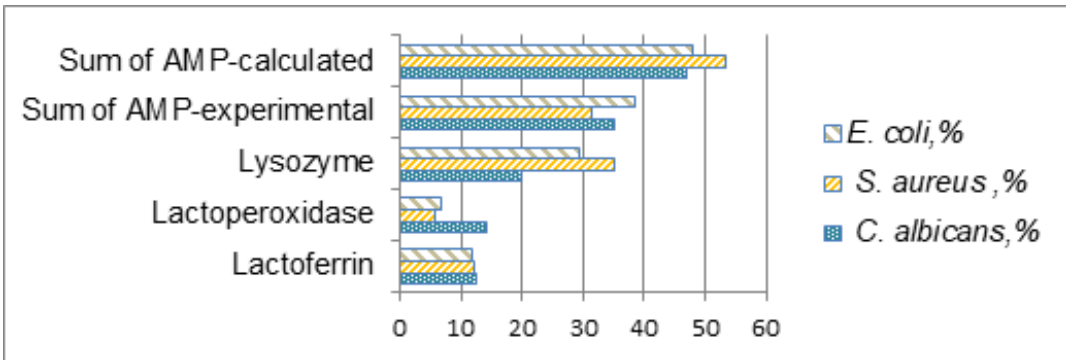

Figure 1. *Microbicidal activity of AMP - lactoferrin, lysozyme, and lactoperoxidase - at concentrations of 5 mg/ml: experimental and calculated values.*

microorganisms. The levels of activity at a drug concentration of 5 mg/ml were: against C. albicans - LF - 12.7%, LP - 14.2%, LC - 20.1%; against S. aureus - LF - 12.4%, LP - 5.8%, LC - 35.3%; against E. coli - LF - 11.9%, LP - 6.8%, LC - 29.5%. A combination of all three drugs (each at a concentration of 5 mg / ml) demonstrated the following activities: against C. albicans - 35.4%; against S. aureus - 31.5%; against E. coli - 38.8%. Obviously, the calculated sum of the activities exceeds the experimental sum of activities of preparations by 1.2 - 1.7 times.

Conclusion: Application of complex AMP in vitro has been shown that the total experimental activity was significantly lower than the calculated sum of the activities of monopreparations. This phenomenon should be notice in case of application of these peptides as antimicrobial drugs.

Biography

Tatiana Kolyganova, Speciality: Epidemiologist, M.D. She is an Assistant of the Department of Microbiology, Virology, and Immunology; First Moscow State Medical University I.M. Sechenov (Sechenov University), Moscow, Russia and Junior Researcher at the Laboratory of Physiology of Fungi and Bacteria, Mechnikov Research Institute for Vaccines and Sera, Moscow, Russia.

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Protein network analysis to prioritize key genes in amyotrophic lateral sclerosis

Shazia Haider and **Rupesh Kumar**

Department of Biotechnology, Jaypee Institute of Information Technology, India

Amyotrophic Lateral Sclerosis (ALS) is a fatal disease, progressive nature characterizes by loss of both upper and lower motor neuron functions. One of the major challenges is to understand the mechanism of ALS multifactorial nature. We aimed to explore some key genes related to ALS through bioinformatics methods for its therapeutic intervention. Here, we applied a systems biology approach involving experimentally validated 148 ALS-associated proteins and construct ALS protein-protein interaction network (ALS-PPIN). The network was further statistically analysed and identified bottleneck-hubs. The network is also subjected to identify modules which could have similar functions. The interaction between the modules and bottleneck-hubs provides the functional regulatory role of the ALS mechanism. The ALS-PPIN demonstrated a hierarchical scale-free nature. We identified 17 bottleneck-hubs, in which CDC5L, SNW1, TP53, SOD1, and VCP were the high degree nodes (hubs) in ALS-PPIN. CDC5L was found to control highly cluster modules and play a vital role in the stability of the overall network followed by SNW1, TP53, SOD1, and VCP. HSPA5 and HSPA8 acting as a common connector for CDC5L and TP53 bottleneck-hubs. The functional and disease association analysis showed ALS has a strong correlation with mRNA processing, protein deubiquitination, and neoplasms, nervous system, immune system disease classes. In the future, biochemical investigation of the observed bottleneck-hubs and their interacting partners could provide a further understanding of their role in the pathophysiology of ALS.

Biography

Shazia Haider received her BSc (Hons) in Zoology from the University of Delhi, and her Ph.D. in the field of Bioinformatics from Jamia Millia Islamia, New Delhi. After postdoctoral research at the Jawaharlal Nehru University, she also worked as an Assistant professor in the Department of Biotechnology, Sharda University and as a Senior research officer (SRO) in the Department of Neurology, AIIMS. She is currently an Assistant Professor, in the Department of Biotechnology, Jaypee Institute of Information Technology (JIIT), Noida, Uttar Pradesh. She has published her paper in a reputed international journal. She was awarded prizes from the Department of Medicine, University of California, San Diego, USA and presented her research work in University of California, Los Angeles, USA and European Bioinformatics Institute (EMBL-EBI), Hinxton, Cambridge, United Kingdom and European Society of Human Genetics, Paris, France. Her research interest is on the specialized field of Bioinformatics and Systems Biology.

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The therapeutic potential of herbal and nano-based herbal therapy against ovarian cancer: New insight into the current evidence

Reza Arefnezhad

Department of Anatomy, Shiraz University of Medical Sciences, Iran

Ovarian Cancer (OCa) is described as one of the common causes of cancer-associated death in women throughout the world. This gynecological cancer is mainly called the "silent killer" because disease manifestations in the early stages are not associated with the OCa. Due to the disease recurrence and resistance to common treatments, finding an effective curative tool against the disease is a puzzle. Based on the reports, some popular herbal formulations, such as curcumin, quercetin, and resveratrol, can have anticancer influences by various mechanisms. However, these herbal products may be along with some pharmacological limitations, like poor bioavailability, instability, and weak water solubility. In contrast, the use of nano-based material, e.g., nanoparticles (NPs), micelles, liposomes, can dramatically overcome these obstacles. Thus, in this review, we will summarize the anticancer aspects of these herbal and-nano-based herbal formulations with a concentration on their action mechanism against OCa.

Biography

Reza Arefnezhad received his BSc degree in surgical technology from Kashan university of medical sciences, and presently I am receiving an MSc degree in anatomical sciences at shiraz university of medical sciences. My interest is in researching immune system-related diseases, especially cancer, herbal medicine, cell therapy.

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Anti-integrins: Is there a future?

Dermot Cox

School of Pharmacy & Biomolecular Science, Royal College of Surgeons, Ireland

The discovery of the integrin cell adhesion family of receptors in the late 1980s created great excitement in the pharmaceutical industry. This family of receptors is implicated in all of the major diseases – cardiovascular disease, cancer and immune disorders. Furthermore, for the first time there were inhibitory monoclonal antibodies available to use as therapeutics. To further ensure success there was a hit compound in the guise of the peptide RGDS that was moderately potent. Thus, as drug targets, integrins had everything going for them. Yet over 30-years later there is little to show for the $billions invested in drug discovery programmes that targeted integrins. The few agents on the market today either have very small sales or are plagued with serious adverse effects.

The reason for the failure of these agents is complex but a common thread was a failure to understand the basic pharmacology of these agents. Drugs that were meant to be antagonists turned out to have agonist-like activity. The pharmacokinetic profiles were not appropriate for oral agents as they had poor bioavilability and short half-lives. Furthermore, due to secrecy within the industry, companies repeated each other's mistakes rather than learning from each other.

Understanding what went wrong with anti-integrin drug discovery programmes is essential to improving the drug discovery process.

Biography

Dermot Cox graduated with a degree in pharmacology and toxicology (University College Dublin) and a PhD in immunology (Dublin City University). I led a drug discovery group in Fujisawa Pharmaceutical Company (Osaka, Japan) working to discover a GPIIb/IIIa antagonist. Subsequently I joined Royal College of Surgeons in Ireland where I have worked on understanding the failure of GPIIb/IIIa antagonists. My current research is on understanding the role of platelets in inflammation and infection (immunothrombosis). I have discovered small molecules that inhibit the immune function of platelets and am working on their development for indications such as sepsis.

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Applications of Bayesian analysis to proof-of-concept trial planning and decision making

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A Proof-of-Concept (PoC) trial is the earliest point in the drug development process at which the weight of evidence suggests that it is "reasonably likely" that the key attributes for success are present, and the key causes of failure are absent. Results from the trial will be used as the basis for critical decision making regarding whether the sponsor will go forward to develop the drug, stop the investment on the drug, or collect additional information and then decide the fate of the compound. To easily communicate the results of a PoC trial to the project team and facilitate quick decision making, various standardized quantitative go and no-go criteria have been proposed by many authors. Criteria of Lalonde et al are based on the comparison of a confidence bar to the target value and lower reference value of the treatment effect and can have a "go," "pause/consider," or "stop/no-go" outcome. Frewer et al evaluate the features of the criteria of Lalonde et al in further details from a frequentist perspective.

Bayesian analysis has advantages over the frequentist analysis allowing the borrowing of historical information through the application of an informative inferential prior in data analysis. It also provides the flexibility for quantifying the treatment effect through the posterior distribution to make probabilistic statements. The latter is particularly important for a PoC study where rather than hypothesis testing, the estimation of the treatment effect should be the focus.

In this presentation, a new approach modifying the criteria of Lalonde et al by shifting some of the "stop" outcomes to "consider" outcomes will be presented. In addition, the application of a Bayesian analysis approach with the use of an inferential prior in data analysis and design priors in trial planning and sample size determination will be illustrated.

Biography

René Kubiak has worked in the pharmaceutical industry for over 25 years. He currently holds the position of Global Head of Early Development and Non-Clinical Biostatistics at Sanofi, where he was instrumental in the implementation of various innovative methods as the quantitative decision-making approaches in Proof-of-Concept studies. Previously, he worked for Boehringer Ingelheim in various statistical positions in early and late phase R&D at sites in Germany and the US. His interest has always been in innovative designs in clinical and non-clinical studies, currently increasingly using historical data or biomarkers. He completed his two degrees in "Statistics" and in "Pharmaceutical Medicine" at the Universities of Dortmund and Basel, respectively.

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In vivo acute toxicity of the biosurfactant mannosylerythritol lipids to swiss mice after intraperitoneal administration

Cristiano José de Andrade[1], Paulo Emilio Feuser[1,2], Ana Letícia Silva Coelho[1], Mariana de Melo Cardoso[2], Rahisa Scussel[2], Gustavo de Bem, Jonathann Correa Possato[2], Bruno Augusto Mattar Carciofi[1], Lariani[2], Ricardo Andrez Machado-de-Ávila[2], Paulo Cesar Lock Silveira[2] and **Debora de Oliveira[1]**

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[2]Postgraduate Program in Health Science, Universidade do Extremo Sul Catarinense, Brazil

At industrial scale, the biosurfactant mannosylerythritol lipids (MELs) are already applied into cosmetic formulations (skincare), however there is also a potential to be used as anti-cancer agent. There are a few studies on the toxicity of biosurfactants, in particular MELs. Therefore, the main of this study was to evaluate in vivo acute toxicity of the homologue mannosylerythritol lipids (MEL B) in Swiss mice, 24 h and 72 h after its intraperitoneal (IP) administration at doses of doses 50 mg/kg and 150 mg/kg. The oxidized intracellular 2',7'-dichlorofluorescein (DCF), sulfhydryl, and superoxide dismutase (SOD) - biochemical parameters - were evaluated in different organs: spleen, lung, liver, kidney, heart, and gastrocnemius. The triglyceride levels, CK-MB and LDH enzymes were also analyzed. The analysis of results demonstrated that the MEL-B administered via IP did not induce acute toxicity in 5 out of 6 organs - except liver, very likely, due to the metabolizing of MEL-B. The triglyceride levels, CK-MB and LDH enzymes did not present any significant alteration. Therefore, the MEL-B is a potential alternative for human formulation, since it showed minimum toxic effects. In addition, further studies are still needed to determine the potential toxic effect of MEL-B in patient.

Biography

Dr. Andrade has plenty of experience on biotechnological processes, in particular fermentation, bacterial metabolism, bioproducts with high surfactant activity, purification processes (ultrafiltration), algae cultivation and green-based extraction methods, and identification of biomolecules by mass spectrometry. Dr. Andrade works as Professor in the Department of Chemical and Food Engineering (EQA)/Federal University of Santa Catarina (UFSC), and also in the Graduate Program in Chemical Engineering at UFSC (PósEnq). Dr. Andrade has published 42 scientific articles, 14 book chapters, and 2 patent deposits.

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March 28-29, 2022

FUTURE PHARMA 2022

A quantum-inspired approach to de-novo drug design

David Snelling

Fujitsu UK, United Kingdom

Design and optimization of targeted drug-like compounds is an important part of the early stage drug discovery process. In this paper, we describe the use of a novel technique for rapid design of lead-like compounds for the Dengue viral RNA-dependent-RNA polymerase (RdRp). Initially, a large (>billions) fragment-based chemical library is designed by mapping relevant pharmacophores to the target binding pocket.

The de-novo synthesis of molecules from fragments is formulated as a quadratic unconstrained binary optimization problem that can be solved using the quantum-inspired Digital Annealer (DA), providing an opportunity to take advantage of this fledgling, ground breaking technology. The DA constrains the search space of molecules with drug-like properties that match the binding pocket and then optimizes for synthetic feasibility and novelty, thus offering significant commercial advantages over existing techniques.

In this session we will present a new technique for de-novo drug design using the quantum-inspired Digital Annealer. The DA improves drug discovery process in two key ways i) it allows for rapid combinational enumeration of billions of possible molecules, larger than any alternatives are able to review. Due to increased evaluated space, the DA is more likely to identify higher quality lead molecules, simply due to the fact that there are vastly more molecules to chose from. ii) despite scanning a broader space, the DA can do so in a fraction of the time needed by alternative solutions, completing single scan of the library, which generates 128 samples, in approximately 0.6 seconds, it is possible to generate thousands of candidate molecules in a matter of minutes. This elucidates the usefulness of technology for successful and rapid design of lead-like components that are synthetically feasible and potentially innovative with respect to existing intellectual properties.

Prediction of the number of infected COVID-19 in the early stages of the epidemic by the embedding method of applied mathematics

Panova Anastasiia Andreevna and **Igor Derevich**

Bauman Moscow State Technical University, Russia

The number of infected COVID-19; variational method; system of ordinary differential equations of relaxation type; universal stages of the COVID-19 epidemic.

Predicting an increase in the number of infected people during an epidemic is an important factor for developing a strategy to combat the pandemic. Reliable forecasts for up to 30 days make it possible to take adequate measures limiting physical social contacts between individuals and provide the population with the necessary medical care. A typical initial epidemic scenario consists of three universal stages. As an example, the initial stages of the development of the COVID-19 epidemic before the start of mass vaccination are considered. In our presentation, these stages are illustrated by examples of an increase in the number of infected in a number of countries in Europe and America.

The first stage is associated with the migration of a significant number of infected people to the country. At this stage, at the initial moment of time, the maximum rate of development of the epidemic is observed. At this uncontrolled stage, the maximum increase in the number of people affected by the coronavirus is recorded. At the second stage, the Governments of the countries take isolation measures that significantly limit physical contact between individuals. At this stage, there is a stabilization of the number of infected. The third stage, caused by the degeneration of viral infection as a result of a sharp decrease in physical contact, was observed only in a few countries with a high level of social responsibility. The initial stages of the epidemic reflect the nature of the social behavior of the country's population. The laws of replication of the original strain of coronavirus, which were the same in all countries, and the peculiarities of the social behavior of the population of countries characterized by significant conservatism, allow using modern mathematics to build reliable forecasts of the number of infected in

the initial period of the Covid-19 pandemic for up to 30 days.

These initial universal stages are analyzed in a presentation based on the variational method of applied mathematics. Предполагается, что рост числа инфицированных описывается системой обыкновенных дифференциальных уравнений. Exponential indicators in these equations change at different stages of the epidemic. The system of equations includes unknown constants, the value of which is estimated on the basis of minimizing the functional equal to the square of the deviation of the total number of calculated and confirmed infected for the entire period of the epidemic. This approach allows us to take into account the conservatism of the social behavior of the population of countries. The minimization of the functional and the calculation of the number of infected are carried out by a joint numerical solution of a system of ordinary differential equations. It turns out that the indicators of the degree of increase in the number of infected at the selected stages are almost constant. This allows you to make forecasts for several days ahead. The effectiveness of the proposed forecasting method is illustrated by comparing it with real data in many countries of the world.

Mutations of virus strains and mass vaccination neutralize the possibilities of local forecasts of the epidemic scenario.

This work was supported by the grants of Russian Foundation for Basic Research No 20-08-01061.

Virtual screening and rational design of antioxidant peptides based on tryptophyllin L structures isolated from the Litoria rubella frog

Thi Thanh Nha Tran[1], Dinh Phien Tran[2], Thi Minh Anh Nguyen[1], Thai Hoang Tran[1], Nu Ngọc Anh Phan[1], Van Cuong Nguyen[1], Van Trong Nguyen[1] and **John H. Bowie[3]**

[1]Industrial University of Ho Chi Minh City, Vietnam

[2]Vietnam-Russia Tropical Centre, Vietnam

[3]The University of Adelaide, Australia

Discovery of natural antioxidants has been carried out for decades relying mainly on experimental approaches which are commonly associated with time and cost demanding biochemical assays. The maturation of quantitative structure activity relationship (QSAR) modelling has provided an alternative approach for searching and designing antioxidant compounds with alleviated costs. As a contribution to this approach, this work aimed to establish a fragment-based 3D-QSAR procedure to discover and design potential antioxidants based on tryptophyllin L structures isolated from the red tree frog Litoria rubella. A Force field and a Gaussian 3D-QSAR model were built to screen for potential antioxidants from tripeptide fragments covering all sequences of tryptophyllin L database. Among those, PWY(NH2) corresponding tryptophyllin L 4.2 was predicted to have the highest 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) radical cation (ABTS+.) scavenging capability. Two newly designed peptides PYW and PYW(NH2) together with PWY(NH2), tryptophyllin L 4.2 and the reference peptide PWY were synthesized and subjected to two antioxidant assays. The ABTS radical scavenging assay revealed that all the tested peptides were strong ABTS+. scavengers with the antioxidant capabilities approximately twice as high as trolox and higher than glutathione. The ferric reducing activities of the peptides were, on the other hand, much weaker than that of trolox suggesting different antioxidant mechanisms inserted by trolox and the peptides.

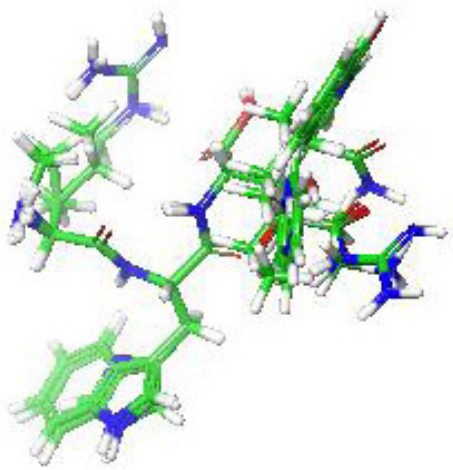

Figure. *Superimposition of 108 peptides from TEAC dataset*

Conc. (μM)	Trolox equivalent antioxidant capacity					
	P-Y-W(NH2)	P-Y-W(OH)	P-W-Y(NH2)	P-W-Y(OH)	L-P-W-Y(NH2)	GSH
2.5	3.25	3.41	3.15	2.94	2.48	2.03
5.0	2.69	2.86	2.71	2.55	2.22	1.76
8.2	2.16	2.31	2.16	2.10	1.92	1.58
10.0	1.92	2.02	1.93	1.89	1.75	1.47

Table. *Trolox equivalent antioxidant capacities of tryptophyllin L 4.1 and its derivatives.`*

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Effect of candesartan and ramipril on liver fibrosis in patients with chronic hepatitis c viral infection: A randomized controlled prospective study

Tarek M. Mostafa[1], Gamal A. El-azab[1], Gamal A. Badra[2], Alyaa S. Abdelwahed[2] and **Abeer A. Elsayed[3]**

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[3]*Department of Clinical Pharmacy, Sinai University, Egypt*

Objective: This study aimed at evaluating the effects of Candesartan and Ramipril on liver fibrosis in patients with chronic hepatitis C.

Methods: This randomized controlled prospective study involved 64 patients with chronic hepatitis C and liver fibrosis. Participants were randomized into three groups; group I (control group; n=21) which received traditional therapy only, group 2 (Ramipril group; n=21) which received traditional therapy plus 1.25 mg/day oral Ramipril and group 3 (Candesartan group; n=22) which received traditional therapy plus 8 mg/day oral Candesartan. Patients were assessed at baseline and 6 months after intervention through measuring of liver stiffness (Fibro-Scan), evaluation of the serum levels of hyaluronic acid (HA) and transforming growth factor-beta 1(TGF-β1) and calculation of indices of liver fibrosis including fibrosis index based on the 4 factors (FIB-4) and aspartate transaminase-to-platelet ratio index (APRI). Data were analyzed using paired t-test and one-way analysis of variance followed by Tukey's HDS test for multiple pairwise comparisons.

Results: At baseline, the three study groups were statistically similar in demographic and laboratory data. After treatment, the three study groups showed significant decrease in liver stiffness, serum levels HA and TGF-β1, and indices of liver fibrosis as compared to baseline data ($p<0.001$). Six-months after treatment, patients on Ramipril and Candesartan showed significant improvement in all measured parameters as compared to control group. Additionally, Candesartan treated group showed significant decrease in liver stiffness, biomarkers and indices of liver fibrosis as compared to Ramipril.

Conclusions: The administration of Ramipril and Candesartan in chronic hepatitis C patients with hepatic fibrosis was well tolerated and effective in improving liver fibrosis. AT1-R antagonist Candesartan maintained anti-fibrotic more effectively than Ramipril and may represent a safe and effective therapeutic strategy for liver fibrosis in patients with chronic liver diseases.

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Effect of probiotics supplementation on disease progression, depression, general health and anthropometric measurements in relapsing-remitting multiple sclerosis patients: A systematic review and meta-analysis of clinical trials

Amir Reza Moravejolahkami[4], Shahrzad Mirashrafi[1], Seyedeh Zahra Hejazi Taghanaki[2], Faezeh Sarlak[3], Mohammad Ali Hojjati Kermani[5] and **Mohsen Haratian[6]**

[1,2,3,4]Isfahan University of Medical Sciences, Iran

[5]Shahid Beheshti University of Medical Sciences, Iran

[6]Hamadan University of medical Sciences, Hamedan, Iran

Background: Probiotics may have a promising role in chronic autoinflammatory diseases. The current systematic review and meta-analysis investigated the effects of probiotics on disease progression, depression, general health and anthropometric measurements in Relapsing-Remitting Multiple Sclerosis (RRMS) patients.

Methods: The English literature search was performed using PubMed, Scopus, Web of Science, and the Central Cochrane Library through January 2021. Random effect models were used to synthesize quantitative data by STATA14.

Results: From a total of 152 identified entries, four trials were included in quantitative synthesis (n=213; 106 as intervention, 107 as control). An additional six studies with the same structure and different markers were also systematically reviewed. The pooled effect size showed that Expanded Disability Status Scale (EDSS) (WMD=-0.43; 95% CI=-0.65, -0.20; P<0.001), Beck Depression Inventory-□ (BDI-□) (WMD=-3.22; 95% CI=-4.38, -2.06; P<0.001) and General Health Questionnaire (GHQ) (WMD=-4.37; 95% CI=-6.43, -2.31; P<0.001) were improved following probiotics supplementation.

However, body weight and body mass index did not statistically change.

Conclusion: Our findings revealed that probiotics supplementation can improve disease progression, suppress depression, and general health in MS patients; although, further investigations may be needed.

Molecular docking study for synthesis of bis-fused system incorporating pyrido[2,3-d] pyrimidine using nano ZnO under microwave condition

Elshimaa Mohmed Eid

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Nano ZnO catalyst used as a green catalyst in synthesis of bis and fused cycles incorporating pyrido[2,3-d]pyrimidine moiety by one-pot, multicomponent reaction of 2,2'-(propane-1,3-diylbis(sulfanediyl))bis(6-aminopyrimidin-4(3H)-one) 3, 1H-indene-1,3(2H)-dione 4 and aromatic aldehydes 5. The reactions carried out using both conventional method and microwave irradaition. Microwave assisted method carried the reaction in 10 min and high yields (89-95%). The Molecular docking simulation study done using PDB: ID (2XVQ) Human serum albumin. The study revealed that compounds strongly fitted into the active sites of the target protein.

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Brucella prostatic abscess: A retrospective study of 8 cases and review of the literature

Hui Guo

Xinjiang Medical University, China

Objective: We aimed to present the clinical characteristic, laboratory test, Magnetic Resonance Imaging (MRI) finding, and treatment with Brucella Prostatic Abscess (BPA).

Methods: The clinical data of eight cases with BPA from December 2013 to December 2019 were retrospectively collected and analyzed. The vocation, age, clinical manifestation, laboratory test, MRI finding, treatment with BPA were summarized objectively.

Results: The median age was 59 years, with a minimum of 43 and a maximum of 63. The common clinical symptom was fever, followed by dysuria, erectile dysfunction, frequent urination, urinate pain. The CRP of all cases increased significantly. The ESR sped up except for one patient. Other laboratory data raised, including monocyte count (50.0%), neutrophil count (25.0%), red blood cell count (25.0%), and white count (25.0%). Prostate enlargement occurred in 87.5% of patients. The lesions located in the peripheral zone (87.5%) and central zone (100%) of the prostate gland. All patients showed a equisignal on T1WI presented a hyperintense signal on STIR. The shape of all lesions was a small nodule or multiple nodules. All patients revealed a slight-hyperintense to hyperintense signal on T2WI and DWI. Three patients had pelvic effusion. Complicated with other organ infections, there were seminal vesicles (37.5%), epididymis (12.5%), and bladder (12.5%). The clinical symptoms of all patients were resolved. All the lesions had disappeared by follow-up ultrasound examinations.

Conclusion: Even in epidemic areas, the incidence of BPA is relatively rare. The result can increase the understanding of BPA and reduce misdiagnosis and mistreatment.

Hematological and biochemical effects of Morinda lucida and Alstonia boonei on the liver and kidney of mice infected with Plasmodium berghei

Olajide Joseph Afolabi and **Eunice Adekemi Abejide**

Federal University of Technology Akure, Nigeria

The present study was undertaken to evaluate the hematological and biochemical effects of the *Morinda lucida* and *Alstonia boonei* in Nigerian traditional medicine for treatment of malaria. The hematological and biochemical activities of the plants against established *Plasmodium berghei* NK65 infection was evaluated in mice treated with extracts of *Morinda lucida, Alstonia boonei*, combined recipe of the plant extracts at graded doses of 400, 600, 800 mg/kg and chloroquine (a standard drug) at 10 mg/kg. The hematological results obtained after 12 days post infection showed that the white blood cell counts of mice treated with 400 mg/kg of *Morinda lucida* and 800 mg/kg of *Alstonia boonei* are significantly higher compared to the untreated group, chloroquine treated and negative control groups. Also, the mean value of hemoglobin per red blood cell is low in infected mice treated with *Alstonia boonei* at 400 mg/kg and the combined recipe of plant extracts at 400 mg/kg compared to other groups such as the group treated with combined recipe of plant extracts at 800 mg/kg and the control group. The biochemical test showed significant increase in mean level of aspartate aminotransferase, alanine aminotrans-ferase, total protein and albumin of all the treatment groups when compared to the control group. Therefore, the isolation and identification of bioactive compounds from these medicinal plants can be explored for obtaining less toxic and effective antimalarial drug.

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Interactions between caveolin-1 (rs3807992) polymorphism and major dietary patterns on cardio-metabolic risk factors among obese and overweight women

Faezeh Abaj and **Kh. Mirzaei**

University of Medical Sciences, Iran

Background: Caveolin-1 (CAV-1) is a cholesterol-dependent essential component located in caveolae. Several studies have been CAV-1 related to cardio-metabolic parameters in animal models, however, there are few studies in humans. Importantly, there is no study has investigated the interaction between *CAV-1 rs3807992* gene and dietary patterns (DPs) on cardio-metabolic risk factors.

Methods: The current cross-sectional study was conducted on 404 overweight and obese women. Dietary intake was obtained from FFQ with 147 items. The CAV-1 genotype was measured by the PCR-RFLP method. The anthropometric measurements, serum lipid profile, and inflammatory markers were measured by standard protocols.

Results: There was a significant interaction between *CAV-1 rs3807992* and healthy DP on high-density cholesterol (HDL) (P-interaction=0.03), TC/HDL (P-interaction=0.03) and high sensitivity C-reactive protein (hs-CRP) (P-interaction=0.04); in A-allele carriers, higher following a healthy DP was related to a higher level of HDL and lower TC/HDL and hs-CRP. As well as, the significant interactions were observed between *CAV-1 rs3807992* and unhealthy DP in relation to triglyceride (TG) (P-interaction = 0.001), aspartate aminotransferase (AST) (P-interaction = 0.01) and monocyte chemoattractant protein-1(MCP-1) (P-interaction = 0.01); A-allele carriers were more following the unhealthy DP had lower levels of TG, AST and MCP-1.

Conclusions: Our study revealed a significant gene-diet interaction between rs3807992 SNPs and DPs in relation to cardio-metabolic risk factors; A-allele carriers might be more sensitive to dietary composition compared to GG homozygotes. Following a healthy DP in A-allele-carriers may be improved their genetic association with cardio-metabolic risk factors.

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Prevalence of hepatitis B e antigenemia in Bahraini hepatitis B patients: A retrospective, single-center study

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[1,2,3]Salmaniya Medical Complex, Bahrain

[4]Ibn AlNafeesa Hospital, Bahrain

Background: Hepatitis B e (HBe) antigen (HBeAg) is commonly encountered among hepatitis B patients and is indicative of active infection. There is a lack of data in the literature about the prevalence of HBeAg among hepatitis B patients in Bahrain and its impact on the disease.

Aim: The aims of this study were to investigate the prevalence of HBeAg among a sample of hepatitis B patients in Bahrain and to analyze their associated laboratory profile, radiological characteristics, comorbidities, and complications.

Methods: This was a retrospective record-review study conducted on patients' records at Salmaniya Medical Complex hospital in Bahrain during the period of 2011-2016. All records of hepatitis B patients who had HBeAg tests performed were included in this study.

Results: Of 323 patients recruited, 18.9% had positive HBeAg. The prevalence of anti-HBe antibodies and hepatitis B core immunoglobulin G (HBc IgG) differed significantly between patients with positive and negative HBeAg ($P < 0.001$, $P = 0.026$, respectively). Alanine transferase and gamma-glutamyl transferase were significantly higher among patients with positive HBeAg ($P = 0.017$, $P = 0.016$, respectively). There was no significant difference with regard to the prevalence of hepatitis C virus, human immunodeficiency virus, hepatocellular carcinoma, or liver transplantation between HBe-positive and -negative patients ($P \geq 0.05$).

Conclusion: HBeAg is prevalent among hepatitis B patients in Bahrain and is associated with a significantly different laboratory profile.

The nobel prized nitric oxide molecule as a noble treatment for nCOVID

Jan Mohammad Mir

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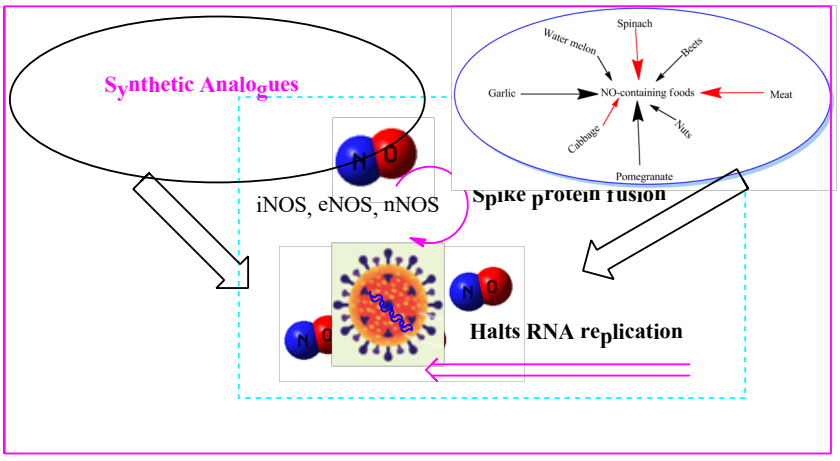
In the prevailing coronavirus disease-2019 (COVID) times, scientists are eager to develop vaccine against COVID-19, and careful measures are being taken to develop an effective drug. Meanwhile, several antiviral compounds have been repurposed for the COVID-19 treatment, and drug repurposing has yielded satisfactory results. In the meantime, NO is also under clinical trials to find its potentiality as anticoronavirus. This work aims to describe the therapeutic potential of nitric oxide (NO) for the treatment of deadly (COVID-19). The significance of NO in mitigating the COVID-19 associated symptomatic complications has also been addressed in this work. So, the profound antiviral effects of NO against coronavirus, and also the role it plays in relieving symptomatic severity of COVID-19 are supportive of the fact to declare NO as a therapeutic option for this disease.



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Impact of IFNL-3 (IL-28B) polymorphism on the kinetics of HBV DNA and qHBsAg and HBsAg clearance during therapy with peginterferon α-2a in patients with HBeAg-negative chronic hepatitis B, genotype D

Sergii V. Fedorchenko, Tatiana Martynovych, Zhanna Klimenko, Olga Liashok, Iryna Solianyk and **Valeriia Reznyk**

The L.V. Gromashevskyi Institute of Epidemiology and Infectious Disease, Ukraine

In recent years baseline predictors of Peg-INF response have been identified, one of the host factors may be include: genetic polymorphism IFNL-3 (IL-28B).

We investigated the effect of IFNL-3 polymorphism (SNP 12979860, SNP rs8099917) on the kinetics of HBV DNA, qHBsAg. At 48 weeks after the end of treatment, the rate of SVR induction, HBsAg clearance, were assessed.

108 patients with HBeAg-negative variant of hepatitis B, genotype D were enrolled into the study. Of 46 patients with CC SNP 12979860, a decline in the concentration of HBsAg ☐ 0.5 log10 at 12 weeks of treatment, was noticed in 23 (50.0%) persons in the group of 61 patients, and in 14 (23.0 %) with CT alleles (P☐ 0.005). In the group of TT SNP rs8099917 alleles carriers (n = 63), a decline in HBsAg concentration ☐ 0.5 log10 at week 12 was achieved in 27 (42.8%), in the TG group (n = 45) - only in 5 (11.1%) (P☐0.001).

HBsAg clearance was documented in 9 (8.3%) of 108 individuals. In 7 of them alleles of CC SNP 12979860 (77.7%) were detected in the general population of patients (n = 108) in 46 (42.6%) (P<0,05) and TT SNP rs8099917 in 8 (88.8%), in the general group – in 63 (58.3%) (P<0,05).

The presented study demonstrates that favorable genetic polymorphism IFNL-3 (SNP 12979860 and SNP rs8099917) is one of the most significant baseline positive predictive factors on SVR induction and HBsAg clearance.

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Reversal of cisplatin resistance by plant derived alkaloids (neferine/ isoliensinine) and their combinatorial regimens with cisplatin induced apoptosis in cisplatin-resistant colon Cancer Stem Cells (CSCs)

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Bharathiar University, India

Objective: Cisplatin chemotherapy to the colorectal cancer cells (CRCs) is accompanied by dose-limiting adverse effects along with acquisition of drug resistance implicating low therapeutic outcome.

Scope and Study: Present study is aimed to evaluate the chemosensitizing efficacy of neferine/isoliensinine or combinatorial regimen of neferine/isoliensinine with cisplatin against CSCs (Cisplatin resistant colon stem cells).

Methods and Results: CSCs were developed using pulse exposure of cisplatin to parental HCT-15 cells. Neferine/isoliensinine or combinatorial regimens of Neferine/isoliensinine and cisplatin exhibited a stronger cytotoxic activity against CSCs compared to control. IC50 doses were found to be 6.5μM for neferine, 12.5μM for isoliensinine, and 120μM for cisplatin respectively. Further, the combinatorial regimen of low dose of cisplatin (40μM) with 4μM neferine/8μM isoliensinine induced cell death in a synergistic manner as described by isobologram. Neferine/isoliensinine could confer extensive intracellular ROS generation in CSCs. Neferine/isoliensinine or combinatorial regimens dissipated mitochondrial membrane potential and enhanced intracellular [Ca2+]i, which were measured by spectroflurimetry. Furthermore, these combinatorial regimen induced significant increase in the sub G0 phase of cell cycle arrest and PI uptake and alleviated the expression of ERCC1 in CSCs. Combinatorial regimens or neferine/isoliensinine treatments down regulated the cell survival protein expression (PI3K/pAkt/mTOR) and activated mitochondria-mediated apoptosis by up-regulating Bax, cytochrome-c, caspase-3, and PARP cleavage expression while down regulating the BCl-2 expression in CSCs.

Conclusion: Our study confirms the chemosensitizing efficacy of neferine/isoliensinine or combinatorial regimens of neferine/isoliensinine with low dose of cisplatin against CSCs.

Therapeutic effect of novel selenium nanoparticles enriched intravesical BCG in mouse model of bladder cancer

Mohammad Hossein Yazdi and **Hoda Shirazi**

Tehran University of Medical Sciences, Iran

Introduction: Intravesical Mycobacterium Bovis bacillus Calmette-Guérin (BCG) therapy for non-muscle invasive bladder cancer has been already applied successfully to prevent metastasis and disease progression. However, some studies have reported a percentage of treatment failure and recurrence along with possible side effects. Therefore, this study has evaluated the effect of administration of synthetic (SSeNPs) and biogenic selenium nanoparticles (BSeNPs) as an adjuvant drugs in combination with intravesical BCG for treatment of mice bearing bladder tumor.

Methods: Orthotopic bladder cancer model mice were established by 12 weeks N-butyl-N-(4-hydroxybutyl) nitrosamine oral gavage. Mice bearing bladder cancer were treated by sequential intravesical treatments with SSeNPs, BCG, BCG/SSeNPs, and BCG/SSeNPs. After immunotherapy, the status of the immune system was evaluated through quantitatively measuring mRNA expression of cytokines by Real-time qRT-PCR in the spleen samples and measuring cytokines protein level by enzyme-linked immunosorbent assay in the serum samples. As well, in the tumor microenvironment, the mRNA expression level of autophagic molecules (Beclin-1, ATG2B, and ATG5), apoptotic molecule (Caspase-3), iNOS, HMGB1, and PD-L1 were evaluated in all groups.

Results: Immunotherapy with BCG/SSeNPs and BCG/BSeNPs elicited a considerable immune response by increasing the expression of IFN-γ, IL-12, and IL-6, and inhibiting the expression of IL-10 and TGF-β cytokines. Along with, BCG/SSeNPs and BCG/BSeNPs could increase Caspase-3 expression and decrease autophagic genes as well as PD-L1.

Conclusion: Our results showed that synthetic and biogenic SeNPs as an effective adjuvant could enhance the efficacy and therapeutic effect of intravesical BCG for bladder cancer treatment with almost the same function.

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Gestational diabetes mellitus is associated with gut microbiota and metabolome

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Objectives/Scope: Gestational Diabetes Mellitus (GDM) is a metabolic disease that occurs in pregnant women and increases the risk for the development of diabetes. This study is to investigate the association between GDM and gut microbiome in the second trimester of pregnancy and meconium, in addition to the alterations in meconium and maternal serum metabolome.

Methods: Healthy pregnant women, GDM patients and their neonates were included in this study. Microbiota of fecal samples of women in the second trimester of pregnancy and their neonates were profiled by 16S rRNA gene sequencing. Meconium and maternal serum metabolome were examined by UPLC-QE.

Results: Our results showed lower α-diversity in gut microbiota of both GDM patients and their neonates. Within GDM patients, seven genera within the phylum Firmicutes and two within the phylum Actinobacteria were significantly decreased, and four genera within phylum Bacteroidetes were increased. In addition, decreased genera within the phylum Firmicutes in GDM patients showed a significant negative correlation with oral glucose tolerance test values. Additionally, microbial gene functions related to glycan biosynthesis and metabolism were found to be enriched in GDM patients. As for neonates of GDM mothers, the abundance of Firmicutes and Proteobacteria changed significantly at the phylum level. Metabolomic analysis of meconium showed that metabolic pathways including taurine and hypotaurine metabolism, pyrimidine metabolism, beta-alanine metabolism, and bile acid biosynthesis were altered in GDM subjects. Several changed metabolites were observed varying by the similar trend across the maternal serum and neonatal meconium.

Conclusions: Our results show the relationship between GDM and gut microbiome in the second trimester of pregnancy and neonates, in addition to the alterations in meconium and maternal serum metabolome, which highlights the importance of maternal factors on early-life metabolism.

Hansen solubility theory in the extraction of policosanol from sugarcane wax

Eduardo Hernández Ramos and **M. De los Ríos**

Cuban Research Institute of Sugarcane Derivatives, Cuba

Policosanol has a recognized efficacy as a treatment for coronary heart disease and its effect as a neuroprotective is being studied in recent articles. Cuba is a pioneer in obtaining this drug from sugar cane; recovering it from a by-product of the sugar production process as part of a mixture of waxy substances. The extraction and refining process of sugar cane wax is based on solvent extraction. The objective of this research is to base changes that improve the sugar cane wax extraction and refining process for the production of policosanol in terms of efficiency, economy, environmental effects and compliance with product quality requirements. Hansen's theory explains in a practical way the affinity that is created between a solute and a solvent. By determining the Hansen solubility parameters, it is possible to analyze the affinity of the solute with different solvents using a tool such as Excel or the Hansen Solubility Practice Parameter Program (HSPiP). From the application of this theory, the solubility parameters that characterize the oil fraction present in the sugar cane wax and the refined wax were obtained. From these results, a criterion was created as to which solvent or solvent mixtures would be suitable for a more in-depth study of the solubility of the wax fractions in them. Independent analysis of the fractions concluded that absolute ethanol is suitable for the extraction of the oil fraction and toluene for the refined wax.

Scaling up red cross peer-supported case hepatitis c case finding to increase entry into pharmacological treatment plans through the red cross movement global hub for community based health in detention

Betts-Symonds G and **E Conroy**

Director Global Hub for Community Based Health in Detention

Irish Red Cross Global Community Based Health in Detention Training Centre, Portloaise, Ireland

This paper starts by acknowledging the success in an Irish Prison using inmate peer educator Red Cross Volunteers in advocating for mass screening in a Major Irish Prison in 2017 (Cowley D, Betts-Symonds G et al) resulting in an 80% uptake and case-finding 17 new cases that were then able to be entered into pharmacological treatment. Objectives, scope, results, methods used and conclusion be discussed,

Building on the success of the 2017 research paper and the creation of a Global Hub for Community Based Health in Detention at Irish Red Cross with an MoU with ICRC and IFRC Geneva, this paper proposes how Community Based Health in Detention that promotes mass peer-supported case-finding can improve access to Hepatitis C treatment throughout the world over the next 20 years.

This paper puts forward the value of the newly formed Global Hub for Community Based Health n Detention consider working with the PHARMA Industry to move forward this important contribution to addressing Hepatitis C in places of Detention.

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Ethnobotanical study of plants used by the traditional healers to treat malaria in Mogovolas district, northern Mozambique

Leonardo Manuel[1], Aurélio Bechel[2], Emília Virgínia Noormahome[3,4,5], Delfina Fernandes Hlashwayo[2] and **Maria do Céu Madureira[6]**

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[6]University of Coimbra, Portugal

Introduction: Malaria is an important parasitic disease that affects mostly the African continent. Traditional medicine is very important in Mozambique and traditional healers play a key role in the primary health care services, particularly in rural areas. We aim to report the results of an ethnobotanical survey undertaken in Mogovolas district, northern region of Mozambique. We recorded and identified the medicinal plants used by traditional healers for treatment of malaria, as well as the mode of preparation and administration.

Methods: The study was conducted in 14 villages from Mogovolas between June and August 2015. Sixteen traditional healers were interviewed using semi-structured questionnaires. Under their guidance, we collected medicinal plants and prepared herbarium specimens that were sent and kept at Eduardo Mondlane University Herbarium for scientific identification. We searched for information on the in vitro and in vivo studies of the cited plants for antiplasmodial activity.

Results: Traditional healers from Mogovolas district reported the use of 37 plants to treat malaria, belonging to 22 families. The most used species are Ochna kirkii, Ehretia amoena and Pteleopsis myrtifolia. These plants belong to Ochnaceae, Boraginaceae and Combretaceae families, respectively. The herbal remedies are prepared using leaves (22/37), roots (18/37), stembarks (16/37) and stems (3/37). The administration of the herbal remedies was made essentially by oral route and bathing.

Conclusion: The ethnobotanical data resulted from this study can be the starting point for further chemical and pharmacological studies aiming to identify medicinal species with antimalarial activity, thus, open the insights for the discovery of new antimalarial substances, as well as better integration of the traditional medicine into the national health systems, particularly in developing countries, as the health system coverage is limited.

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Effect of patient-led cooperative follow-up by general practitioners and community pharmacists on osteoporosis treatment persistence

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Rheumatologist, France

Aim: Osteoporosis is a major risk factor for fractures. Poor persistence with osteoporosis medication hampers outcomes. This study assessed whether encouraging the formation of patient-led follow-up cooperatives between general practitioners (GPs) and community pharmacists improved medication persistence.

Methods: All consecutive patients who attended an osteoporosis patient education program were invited to participate. They were given a logbook containing questionnaires they would bring to 6-monthly visits to their GP and pharmacist. The effect of this 3-year cooperative follow-up on persistence with medication and lifestyle changes was assessed.

Results: In total, 121 patients (average age, 67 years; 93% female) participated. Poor cooperation between GPs and pharmacists was noted. Nevertheless, medication persistence ranged from 83% to 91% over the 6 visits. However, since patient drop-out rates were high and questionnaire return rates were low, a post-study medical chart review was performed. This confirmed that persistence was high (74%-83%) at 3 years post-enrollment, even for oral bisphosphonate-treated patients (73%-76%). However, adoption of anti-osteoporosis lifestyle changes was poor throughout the study: one- to two-thirds of the patients did not alter their diet, physical activity, or surroundings to prevent falls.

Conclusion: One study goal, namely, to encourage GPs and pharmacists to cooperate in patient follow-up, was not achieved. However, high medication persistence was observed. This may reflect the education program, patient empowerment, personalized attention from study personnel, and being in a study. Patient-centered approaches can thus significantly increase medication persistence in osteoporosis. Ongoing education may be needed to improve patient adoption of and persistence with lifestyle changes.

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Effects of hypothermia and pentoxifylline on the adnexal torsion/detorsion injuries in a rat testis model

Reza Elmimehr[1], Ali Motamed-Sanaye[2], Balal Brazvan[3], Seyed-Hosein Abtahi-Eivary[4], Maryam Moghimian[5] and **Masoumeh Fani[3]**

[1,2,3,4,5]*Gonabad University of Medical Sciences, Iran*

Scope: Testicular torsion is surgical urogenital emergency. Hypothermia has been successfully employed in preserving the viability of ischemic organs. Pentoxifylline a xanthine derivative could be used as a drug inhibiting the inflammatory factors.

Objective: The present experimental research utilized a testicular torsion/detorsion model in the male rats for determining the impact of pentoxifylline (PTX) and hypothermia on the male fertility factors.

Methods: 40 mature male wistar rats have been equally randomly categorized into five groups, including: Sham; testicular torsion followed by detorsion (TD); torsion and detorsion with Hypothermia (TD+ICE); testicular torsion/detorsion received (40 mg/kg) of pentoxifylline (TD+PTX); torsion and detorsion with hypothermia plus PTX (40mg/kg) (TD + ICE + PTX). Under anesthesia Left testicular torsion has been performed for 4 hours and 30 minutes before detorsion, PTX has been injected intraperitoneally to groups 3 and 5 and ice fragments have been used to groups 2 and 5 from the beginning of torsion. Finally, after reperfusion period (a week), biochemical, hormonal, sperm parameter, histopathological, and gene expression evaluations have been performed on the blood and tissue samples.

Results: Outputs indicated significant negative changes in the TD group for histological variables, rate of sperm, oxidative marker's serum levels, testosterone hormone, BCL2 and Caspase3 expression. In most cases, the parameters studied in the group receiving PTX improved compared to the TD group, while the results in the hypothermia group showed more damage than in the TD group, and similarly in the group who received PTX+ICE had more damage than the TD group. However, these changes have been not significant in most cases.

Conclusion: The obtained results revealed that using of PTX can to a large extent help maintain fertility while hypothermia has negative effects. Moreover, the combination of these two has increased the damage in most cases, which can be due to the duration of cold use.

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Optimal PD-type networked iterative learning algorithm based fault estimation for repetitive systems with delays, packet losses, sensor saturation and sensor failure

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[2]Advanced Teacher is Training College for Technical Education, University of Douala, Cameroon

For a class of repetitive Networked Control Systems (NCSs) with packet loss, network-induced delays, bounded disturbances, additive sensor saturation constraint and sensor failure, an optimal proportional derivative-type (PD-Type) iterative learning algorithm (ILA) based sensor fault estimation (FE) is designed with the aim to evaluate and estimate the effect of sensor fault on system between every iteration. To do so, state variables, Markov chain process of random packet losses, network-induced delays, bounded disturbances, additive sensor saturation constraint and sensor failure are introduced to establish an extendedstate-space system model. Then, based on this model, the iterative learning algorithm ILA based sensor FE is designed. Using the linear matrix inequalities (LMIs) technique for linear repetitive processes, sufficient conditions are developed with the Lyapunov Krasovskii technique and H∞ approach to calculate the iterative learning gain matrices and the observer gain matrix. In addition, MATLAB optimization based on YALMIP is applied to improve the performance of proposed scheme. Finally, the feasibility and effectiveness of the proposed design method is illustrated on a networked dynamic hydro-turbine governor system based on Matlab/Simulink and TrueTime toolbox.

Novel application of Bismuth Oxide nanoparticles in intraoperative radiotherapy

Zahra Alyani Nezhad and **Ghazale Geraily**

Tehran University of Medical Sciences, Iran

Purpose: Intraoperative radiotherapy (IORT) technique is an advanced radio therapeutic method used to deliver a high single dose radiation during surgery while removing healthy tissues from the radiation field. Nowadays, growing attention is being paid to IORT for its low energy (kilovoltage) delivery as it requires less radiation protection, but suffers several disadvantages, including high-dose delivery and prolonged treatment time. The application of nanoparticles with high atomic number and high attenuation coefficients in kilovoltage energy may help overcome the mentioned shortcomings. This study was designed to investigate and quantify the mean Dose Enhancement Factor (DEF) in the presence of nanoparticles using IORT method. Methods: Bismuth oxide nanoparticles (Bi2O3NPs), both in sheet and spherical formats, were synthesized using a novel hydrothermal method and characterized with X-ray Diffraction (XRD), transmission electron microscopy (TEM) and Brunauer-Emmett-Teller (BET) analysis. Genipin-gelatin gel dosimeter (GENIPIN) was produced in three batches of pure, with sheet and with spherical nanoparticles in concentration of 46.596 µg/ml, and irradiated with 50 kV X-rays. Results: Samples were scanned by a spectrophotometer, which indicated a DEF of 3.28±0.37 and 2.50±0.23 for sheet and spherical NPs, respectively. According to the results of this study, GENIPIN is a suitable dosimeter for the evaluation of three-dimensional dose distribution in the presence Bi2O3 NPs. Conclusion: As a result, IORT along with Bi2O3 NPs has the potential to reduce treatment time and/or normal tissue dose; moreover, it could provide localized dose enhancement.

DNA nanotechnology for modulating the growth and development of neurons

Mirza Muhammad Faran Ashraf Baig

The University of Hong Kong, Hong Kong

Late prenatal growth, early postnatal growth, and layering of the neocortical neurons (NC-Ns) play

determining roles in the development of the cerebral cortex (CC). Here, we systematically explore the interactive role of neuronal surface receptors (NSRs) on cytoskeleton activation (CA) and the

piconewton (pN) force generation (P-FG) and their influence on the proper development, growth,

and functioning of neurons using a designed DNA nanomechanical device (DNA-NMD).

This DNA-NMD, functioning as a molecular tension probe (MTP), can be used to selectively

bind the different NSRs (β-NGFR, Reelin, and Integrin) to mono-, bi-, and trispecifically activate

the receptors on the NC-Ns surface for imaging and calculating the P-FG involved in various

processes. Measurements in vivo on the brain of newly born Institute of Cancer Research mice

(early postnatal) or in vitro after extracting neurons from the fetal brain of pregnant Institute of

Cancer Research mice (late prenatal) reveal that there are augmented interactive roles of the

β-NGFR with Integrin and Reelin receptors (RR) on the CA and P-FG, resulting in enhanced

directional migration of the neuronal endings (M-NEs), layering, and the somal terminal

translocation (S-TT) followed by early postnatal growth.

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