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VIRTUAL EVENT

ADVANCES IN MEDICINAL CHEMISTRY AND PHARMACOLOGY

&

INNOVATIONS IN DRUG DISCOVERY, DEVELOPMENT & DELIVERY

2025

APRIL 04

SCIENTIFIC PROGRAM

APRIL 04, 2025

Greenwich Mean Time

08:00-08:10	**Introduction**

Sessions: Medicinal Chemistry | Drug Discovery, Design and Development | Novel Drug Delivery Systems | Computer Aided Drug Design | Pharmacogenomics and Personalized Medicine | Orphan Drugs and Rare Diseases | Molecular Docking and Computational Drug Design | Biologics and Biosimilars | Drug Safety and Pharmacovigilance | Personalized Therapies | Pharmacogenomics | Toxicology

Distinguished Speaker Talks

08:10-08:30	Title: Water Clarification and Impact Transfer on Tissues in Wet Contact **Juhani H. Pylkkanen,** *SansOx Ltd., Switzerland*
08:30-08:50	Title: Smart Epoxy Coatings: Revolutionizing Metal Protection with Self-Healing and Multifunctional Capabilities using Biopolymers **Demian I. Njoku,** *Hong Kong Metropolitan University, China*
08:50-09:10	Title: Effects of Leukocyte- and Platelet-Rich Fibrin on Diabetic Foot Ulcers: A Retrospective Study **Fen Wang,** *Tongji Hospital, Huazhong University of Science and Technology, China*
09:10-09:30	Title: Primary Side Effect Mechanisms of Covid-19 Vaccines and Serious Pathologies **Beril Anilanmert,** *Istanbul University-Cerrahpasa, Turkiye*
09:30-09:50	Title: Anomaly Detection in Drug Discovery **Ekin Can Erkuş,** *Huawei Technologies, Turkey R&D Center, Türkiye*
09:50-10:10	Title: Mutagenic Azido Impurities in Drug Substances: A Perspective **Sumit Sunil Chourasiya,** *IOL Chemicals and Pharmaceutical Ltd., India*
10:10-10:30	Title: Exploration of Cultivable Actinomycetes in Producing Extracellular Enzymes and their Therapeutic Applications **Jayachandra S. Yaradoddi,** *Basaveshwar Engineering College, India*

REFRESHMENT BREAK 10:30-10:45	
10:45-11:05	Title: Early-Stage Detection of Furcation Radiolucency in Primary Mandibular Molars using Vision Transformer **Naveen Aggarwal,** *UIET-Panjab University, India*
11:05-11:25	Title: Triclosan-Induced Histopathological Alterations, Oxidative Stress and Immune Dysfunction in the Skin of the Fish, *Cyprinus carpio* **Usha Kumari,** *Banaras Hindu University, India*
11:25-11:45	Title: Acoustic Wave-Enhanced Disruption of Cellular Membranes: Implications for Medicinal Chemistry and Diagnostics **Sushama Agarwalla,** *Indian Institute of Technology Hyderabad, India*
11:45-12:05	Title: Antimicrobial Potential of *Potentilla indica* (Andrews) Th. Wolf Extracts against ESKAPE Pathogens and *Candida albicans*: A Step Towards Combating Antimicrobial Resistance **Dimple Guleria,** *Himachal Pradesh University, India*
12:05-12:25	Title: Nrf2 a Novel Target of Cancer Treatment **Muhammad Haidar Zaman,** *Abasyn University, Pakistan*
12:25-12:45	Title: Impact of Green Pathways on Memory and Cognition: Identification of Potential Therapeutic Agents for Alzheimer's Disease to Improve Mental Health **Mehreen Lateef,** *Bahria University College of Allied Health Sciences, Pakistan*
12:45-13:05	Title: A Randomized, Double-Blind, Placeo-Controlled Trial Assessing the Efficacy and Safety of a Fixed-Dose Combination (FDC) of MEtformin Hydrochloride 1000 mg ER, SItagliptin Phosphate 100 mg and DApagliflozin Propanediol 10 mg in Indian Adults with Type 2 Diabetes: The MESIDA Trial **Akhilesh Sharma,** *Alkem Laboratories Mumbai, India*
LUNCH BREAK 13:05-13:25	
13:25-13:45	Title: Assessment of the Antileishmanial Activity of Diallyl Sulfide Combined with Meglumine Antimoniate on *Leishmania major*: Molecular Docking *in vitro* and Animal Model **Farzaneh Zarrinkar,** *Kerman University of Medical Sciences, Iran*
13:45-14:05	Title: Novel Effect of Topical Roquinimex and its Combination with Clobetasol on an Imiquimod-Induced Model of Psoriasis in Mice **Abeer Mohammed Hasan Garma,** *Uruk University, Iraq*

14.05-14.25	Title: Sodium Citrate Buffer Improves Pazopanib Solubility and Absorption in Gastric Acid-Suppressed Rat Model **Huda Jassim Muhammad,** *Karbala University, Iraq*
14:25-14:45	Title: Effect of *Melia azedarach* Seed Mediated Nano-ZnO on Growth Performance, Protein Utilisation Efficiency, Haematology and Nutritional Status in Pigs **Enathi Dinga,** *North West University, South Africa*
14:45-15:05	Title: Social Determinants for the use of Complementary and Alternative Therapies among Women During Pregnancy, Labor and Postpartum Period in Low Income Countries: A Scoping Review **Mabel Kefilwe M. Magowe,** *University of Botswana, Botswana*
15:05-15:45	Title: Silver Nanoparticles as SERS Substrates for Enhanced Raman Spectroscopy in Antimicrobial Drug Analysis Title: Advancing Vibrational Spectroscopy for Biomedical Applications **Maria Cristina Gamberini,** *University of Modena and Reggio Emilia, Italy*
Refreshment Break 15:45-16:00	
16:00-16:20	Title: The Creative Process in Scientific Discovery **Albert Rothenberg,** *Harvard Medical School, USA*
16:20-16:40	Title: Novel Small Molecules Mimic Molecular and Protective Effects of Dietary Restriction to Inhibit Proteotoxicity and Inflammation and Increase Lifespan **Charles Mobbs,** *Icahn School of Medicine at Mount Sinai, USA*
16:40-17:00	Title: Discovery of Antibodies that Modulate Macrophage Functions in Boosting Cancer Immunotherapy **Jianyong Wang,** *Genentech, USA*
17:00-17.20	Title: Guiding the Repair Process **Marcos Barbosa Salles,** *Marcelo Yoshimoto Institute, Brazil*
17:20-17.40	Title: Human Plasma Kallikrein/Kinin and Plasminogen Activation Systems: A Crosstalk in Breast Cancer **Guacyara da Motta,** *Universidade Federal de São Paulo, Brazil*
17:40-18.00	Title: Comparing the Generalizability of Reliability-Based vs. Accuracy-Based Diagnostic Models in Medical and Healthcare Applications **Sepideh Etemadi,** *University of Minnesota Duluth, USA*
NETWORKING	

BOOKMARK YOUR DATES

7th Global Summit on

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INNOVATIONS IN DRUG DISCOVERY, DEVELOPMENT & DELIVERY

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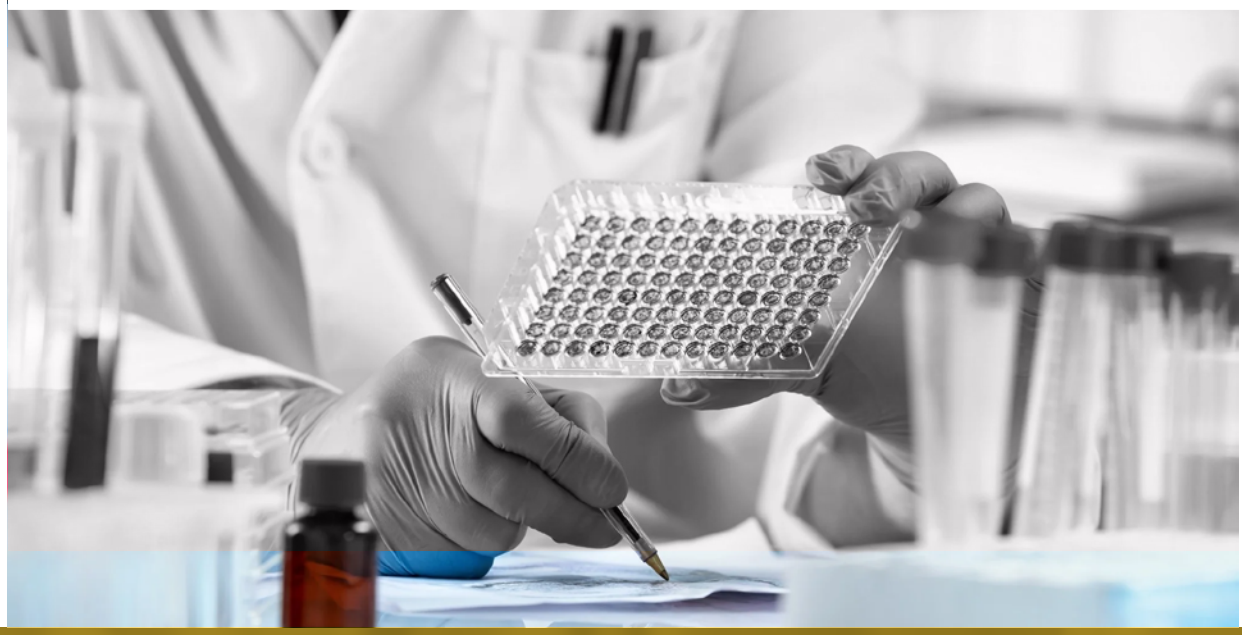


VIRTUAL EVENT

JOINT EVENT

ADVANCES IN MEDICINAL CHEMISTRY AND PHARMACOLOGY

&

INNOVATIONS IN DRUG DISCOVERY, DEVELOPMENT & DELIVERY

APRIL 04, 2025

SPEAKER TALKS

Water Clarification and Impact Transfer on Tissues in Wet Contact

Juhani Pylkkanen

Professor, Chief Engineer, SansOx Ltd., Switzerland

Water is a pure substance that picks up a huge load during its cycles on the earth, bio systems, in washing and cleaning, as well as in industrial and agricultural processes. Water can be clarified and loaded again with desirable gases like clean air within seconds by the new integrated clarification technology in tube condition. The clarified and reloaded water is able to transfer impact of the load on tissues in wet contact, and pick in slag from the tissue due to reduced surface tension. The water clarification technology is presented briefly, and selective case studies of air impact transfer on bio tissues in wet contact are reported briefly here.

OxTube, a new water treatment innovations, clarifies water matrices in tube condition within seconds by four seamless phases; (1) separation of dissolved substances, (2) activation of molecules, (3) clarification and (4) post dissolving and refreshing. It separates and removes dissolved gases like radon, carbon dioxide, hydrogen sulfide and hydrocarbon, and dissolved solids like iron, manganese compounds, calcium, fluorine and phosphorus within seconds. Combined removal of pharmaceutical residues, disinfection and clarification in one within seconds is verified by ozone feed. Efficiency is based on kinetic energy of the flow converted to high dynamic pressure, even mixing and high collision probability of molecules in tube condition.

Health and wellness impacts of clean air can be dissolved in to the water such a way that exchange of slag and air gas between bio systems and the water initiates immediately in wet contact. Comparable iron gets rusted right away in this treated water but it could take years in dry air.

Biography

Chief Engineer, Professor Juhani Pylkkanen, education on Mechanical Engineering, Machine Design, Manufacturing Technology and Enterprise Economics, major positions Professor on Production technology at Oulu University, SVP Technology at ABB, Head of ABB Corporate Research Center Finland, VP Technology at Agco Valtra, VP Technology at Moventas Oy, Head of Production Development at Wartsila Diesel, Machine Tool Designer at Yasuda Industry Japan, Major Publications on Water Treatment Technology, Factory Automation, Unmanned Manufacturing, Flexible Manufacturing Systems, Numerical Controlled Machining, Lean Manufacturing and Quality Assurance.

Smart Epoxy Coatings: Revolutionizing Metal Protection with Self-Healing and Multifunctional Capabilities Using Biopolymers

Demian I. Njoku[1,2,3] and **Annuncieta C. Njoku**[4]

[1]Department of Applied Science, School of Science and Engineering, Hong Kong Metropolitan University, China

[2]Corrosion and Protection Division, Shenyang National Laboratory for Materials Science, Institute of Metal Research, Chinese Academy of Sciences, China

[3]Africa Centre of Excellence in Future Energies and Electrochemical Systems (ACE-FUELS), Federal University of Technology Owerri, Nigeria

[4]Department of Polymer and Textile Engineering, Federal University of Technology Owerri, Nigeria

Unexpected material failures caused by coating layer issues can lead to severe consequences, including compromised structural integrity, safety hazards, significant economic losses, environmental damage, and harm to reputation. In critical applications such as aerospace, automotive, and industrial settings, the risks are particularly high, underscoring the importance of rigorous coating selection, application, and maintenance to ensure long-term performance and reliability. The present report explores the process of developing advanced functional epoxy-based coatings designed to mimic the human healing process in their defect-repairing process. This capability reduces the risk of failures due to unforeseen physical impacts on various metal substrates. The innovative strategy involves the loading of bioderived anticorrosive agents in the lumen of mineral-derived nano-containers interfacial modified with biopolymer-based hydrogels. The coatings respond sensitively to external stimuli typical of corrosive environments which significantly enhances the protection of carbon steel in marine environments. Long-term spectroscopic analyses, impedance measurements, local electrochemical tests, and the assessments of mechanical and physical properties have validated these enhancements. Our findings underscore the potential of advanced epoxy-based coatings to provide durable, multifunctional protection for metal substrates in harsh marine conditions, especially, the ability to autonomously recover after unexpected physical insults in the coating layer matrix.

Biography

Demian I. Njoku holds a PhD in Materials Science and Engineering from the University of Chinese Academy of Sciences, earned in 2018. He also possesses an M.Sc. and a B.Sc. in Chemistry, with specializations in Environmental and Industrial options. Currently, he is a Research Associate at the School of Science and Technology, Hong Kong Metropolitan University. Before this role, he served as a Special Research Assistant at the Institute of Metal Research, Chinese Academy of Sciences, and held faculty positions at ACEFUELS-FUTO and Madonna University in Nigeria. His research interests encompass functional coatings, paper-based microfluidic devices, environmental science, computational studies, smart polymeric composites, pathogen-capturing materials, and corrosion-mitigating strategies.

Effects of Leukocyte- and Platelet-Rich Fibrin on Diabetic Foot Ulcers: A Retrospective Study

Fen Wang[1,2], Xiaoling Zhang[1,2], Jing Zhang[1,2], Song Gong[1,2], Jing Tao[1,2], Hui Xiang[1,2], Xiaoqing Fu[1,2], Xuna Bian[1,2], Xuefeng Yu[1,2], Anhui Xu3, Chengla Y[i,4] and **Shiying Shao[1,2]**

[1]Division of Endocrinology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, China

[2]Branch of National Clinical Research Center for Metabolic Diseases, China

[3]Division of Radiology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, China

[4]Division of Trauma Surgery, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, China

Background: Diabetic foot ulcer (DFU) is one of the most serious complications in diabetes. Leukocyte- and platelet-rich fibrin (L-PRF) is a next generation of autologous platelet-rich plasma. This study is aimed to investigate the clinical effects of L-PRF in diabetic patients in real clinical practice.

Methods: DFU patients who accepted L-PRF treatment and meet the inclusion criteria and exclusion criteria from 2018 to 2019 in Tongji Hospital were enrolled. The clinical features, wound evaluation, treatment of DFU, assessment of therapeutic effectiveness and images of ulcers were retrospectively extracted and analyzed. L-PRF treatment was performed every 7 ± 2 days until the ulcer achieved complete epithelialization or a more than 80% overall percentage volume reduction (PVR). Overall PVR, overall healing rate and weekly healing rate were the main evaluation index.

Results: There are 26 DFU patients enrolled with the ulcer duration 47.0 (35.0, 72.3) days. The severity and infection of ulcers varied with SINBAD score ranging from 2 to 6, Wagner grade ranging from 1 to 4, and PEDIS score ranging from 2 to 4. The initial ulcer volume before L-PRF treatment was 4.94 (1.50, 13.83) cm^3 and the final ulcer volume was 0.35 (0.03, 1.76) cm^3. The median frequency of L-PRF therapy was 3 (2, 5). There were 11 patients who achieved complete epithelialization after the fifth therapy and 19 patients who achieved equal to or more than

80% volume reduction at the seventh week of L-PRF treatment. The overall wound healing rate was 1.47 (0.63, 3.29) cm^3/week and the healing rate of the first two weeks were faster than that of the remaining weeks. Concurrent medicines did not change the percentage of complete epithelialization and the healing rate.

Conclusions: Adding L-PRF to SOC significantly improved wound healing in DFU patients independent of ABI index, SINBAD or Wagner grade.

Biography

Fen Wang, received Medical Doctor degree in Internal Medicine from Peking Union Medical College Hospital, Beijing, China in 2018.

Primary Side Effect Mechanisms of Covid-19 Vaccines and Serious Pathologies

Beril Anilanmert, Gulten Rayimoglu and **Fatma Cavus Yonar**

Institute of Forensic Sciences and Legal Medicine, Istanbul University-Cerrahpasa, Turkiye

Most of the current SARS-CoV-2 vaccines are based on producing or introducing the spike (S) protein, which is responsible from the main pathology of vaccines and even COVID-19. It causes pathologies due to hypercoagulable state, hyperinflammation, autoimmune reactions and cell damages in the organs or systems where it is localized. To assess the side effects experienced after vaccinations, the mechanisms of the spike proteins introduced by the vaccines should be evaluated. The primary pathological mechanisms and some serious side effects are presented under the light of literature.

Spike protein has multiple pathways of causing pathologies: After it binds to Angiotensin Converting Enzyme2 (ACE2), fusion peptide is released after a series of cleavages of spike protein. Synctia occurs *via* the pores formed by the aid of fusion peptide [1]. Different lymphocytes remain inside syncytia to form cell-in-cell structure and such cells die rapidly. Downregulation of ACE2 by spike protein causes dysregulation of the renin–angiotensin–aldosterone system (RAAS) which increases pulmonary vasoconstriction and induction of tissue factor (TF) and plasminogen activator inhibitor 1 (PAI-1) expression on platelets and the endothelium. Endothelial cell damage, immunothrombosis or thromboinflammation, hypertension occurs. Immune response is dysregulated and the hyperinflammation appears, proinflammatory cytokines, particularly IL-6 and TNFα are overproduced. Spike protein act as infectious prion-like protein, which can replicate using PrPC (*via* inducing misfolding in normal variants of the same protein). It also crosses the human brain endothelial cell barrier effectively, while it can exist in peripheral blood monocytes for 15 months. Spike used some vaccines has been made less fusogenic, however, none of the vaccine inventors mutated the S2' site of the protein, which releases the fusion peptide after its breakage.

RNA molecule is unstable, however mRNA vaccines are attached to lipid nanoparticles, graphene etc. for stability. The composition of the lipid nanoparticles, the formulation components, the sequence selection for the vaccine mRNA and the amount of RNA also may influence the

side-effect profile. While the ratio is 36% in natural SARS-CoV-2 virus, mRNA exists in the most well known two mRNA vaccines in a ratio of 53% and 61% with higher reactogenity. Replacing uridines with pseudouridines or methyl-pseudouridine, overcomes the recognition of mRNA by the Toll-Like Receptors, so mRNA can progress into cell easily. This replacement and addition of a long poly(A) tail and the 30 UTR from human globin stabilizes and improve its translation.

mRNA was shown to replicate itself in 6 hours *via* endogenous reverse transcriptase in hepatic cells upon mRNA vaccine exposure [2]. mRNA vaccines strongly trigger IFN-I. Especially after multiple administration, IFN-I can also lead to depression, cognitive slowing and cause symptoms of chronic fatigue syndrome and stimulation of synthesis of cytokines and chemokines.

Pathologies occur in the sites where the spike proteins are more localized. Dyspnea, deep fatigue, headache and muscle/joint pains, extremity weakness, reduced mental clarity/concentration, heat/cold intolerance, menstrual changes and palpitations are among the mild and most frequent side effects of these vaccines. However, it should not be forgotten that such symptoms may be related with more serious vaccine pathologies related to cerebrovascular, kidney, heart diseases, etc., even Long Covid. Among the more reported serious adverse events with fatal income after COVID-19 vaccination, there were anaphylaxis, myocarditis, Guillain–Barré Syndrome (GBS) acute transverse myelitis (TM) and a specific pathology called vaccine-induced thrombotic thrombocytopenia (VITT), which has been arised after vaccination period. Serious side effects also include; kidney injuries, facial (Bell's) palsy, autoimmune hepatitis, Creutzfeldt-Jakob disease, and even cancers as lymphoblastic leukaemia/lymphoblastic lymphoma and axillary lymphadenopathy.

Serious side effects are regarded as low, however, regarding the pharmacovigilance aspect, reporting rate is low among both health professionals and public and there are a well amount of unreported adverse events. Also in the mass vaccination period, most of the studies compared the vaccinated, with the unvaccinated infected population, instead of unvaccinated healthy+infected population. Of course, this was another reason that dropped the real rate of vaccine induced pathologies and fatalities.

Biography

Associate Professor Dr. Beril ANILANMERT is a pharmacist and working in Istanbul University-Cerrahpasa, Institute of Forensic Sciences and Legal Medicine, she has two PhD's one is in Analytical Chemistry and 2nd is in Forensic Sciences. She has received Associate professorship degree in 2017. She has studies in the area of method development for detecting drugs in drug facilitated crimes, analysis of psychoactive and toxic substances, DNA, and explosives, 17025 Laboratory Accreditation and the interaction of cancer drugs. She has performed literature reviews on forensic pharmacy: side effects of the vaccines from a pharmacovigilance aspect. She has 8 book chapters with well-regarded publishers and 19 indexed publications and 2 patents related to drug analysis. She has performed more than 150 reviewer tasks in Sci Indexed journals. Her H-index is 7 and has 152 citations in ISI Web of science.

Anomaly Detection in Drug Discovery

Ekin Can Erkuş

Huawei Technologies, Turkey R&D Center, Intelligent Application DC, Türkiye

Anomaly detection is an important aspect of drug discovery, as it allows researchers to uncover unexpected patterns and deviations, which can provide useful knowledge about drug safety, effectiveness, and behavior. Techniques designed specifically for time series data are especially useful, as they help overcome the difficulties of analyzing high-dimensional datasets that are common in pharmaceutical research. For example, by using sliding window methods along with ways to measure differences, small and short-term problems in changing datasets can be found. By focusing on smaller parts of the data, these methods can identify unusual patterns those older methods might miss, which is particularly useful in fields like studying how drugs work in the body and how people respond to them. This is important because even tiny changes can give important clues about what is happening inside the body, and even minor anomalies in these contexts may reflect important biological processes. Consequently, time-dependent interactions relevant to drug development can be better understood when such deviations are measured accurately.

Time series analysis is useful for detecting patterns and causal relationships over time, which are important in drug discovery research. It is especially useful in the early stages of drug development, such as predicting side effects, because identifying unusual patterns can provide important insights for decision-making. Recent studies suggest that time series approaches can produce more consistent results and improve the drug discovery process. Furthermore, merging several forms of data or using machine learning models can aid anomaly detection performances even further. Therefore, utilizing time series and anomaly detection approaches in drug discovery not only makes it easier to analyze complex data but also help to build safer and more effective therapies.

Biography

Dr. Ekin Can Erkuş holds a Ph.D. in Biomedical Engineering from Middle East Technical University, where his research focused on collective anomaly detection in time series data. He also earned an M.Sc. from the same institution and a B.Sc. in Electrical and Electronics Engineering from Hacettepe University. His technical expertise includes biomedical signal processing, artificial intelligence, machine learning, and time series analysis. He currently works as a Senior AI Research Engineer, Team Lead and Academic Research Manager at Huawei Technologies, where he leads projects on search and recommender systems, AI model development, and feature engineering. Throughout his academic and professional career, he has published numerous research papers and book chapters, advancing fields such as anomaly detection and biomedical data analysis.

Mutagenic Azido Impurities in Drug Substances: A Perspective

Sumit S. Chourasiya[1], Deepika Kathuria[2], Vipin Kumar[1] and **Kamlesh J. Ranbhan[1]**

[1]Department of Process Research and Development, IOL Chemicals and Pharmaceutical Ltd., India.
[2]University Centre for Research and Development, Chandigarh University, India

Contamination of drug products and substances containing impurities is a significant concern in the pharmaceutical industry because it may impact the quality and safety of medicinal products. Special attention is required when mutagenic impurities are present in pharmaceuticals, as they may pose a risk of carcinogenicity to humans. Therefore, controlling potential mutagenic impurities in active pharmaceutical ingredients (APIs) to an acceptable safety limit is mandatory to ensure patient safety. As per the International Council for Harmonization (ICH) M7(R2)[3] Guideline, mutagenic impurities are those compounds or materials that induce point mutations. In 2018, the sartan class of drugs was recalled due to the presence of N-nitrosamine impurities, which are potential mutagens. In addition to the primary impurities being detected, this class of products, especially losartan, irbesartan and valsartan, have been identified as having organic azido contaminants, which are again highly reactive toward DNA, leading to an increased risk of cancer. These azido impurities form during the preparation of the tetrazole moiety *via* the reaction of a nitrile intermediate with sodium azide. Given that this is a newly raised issue in the pharmaceutical world, it should be noteworthy to review the related literature. Thus, this review article critically accounts for (i) the toxicity of azido impurities and the proposed mechanism of mutagenicity, (ii) the regulatory perspective, and (iii) the sources and control strategies used during the preparation of drug substances and (iv) future perspectives.

Biography

Dr. Sumit S. Chourasiya was born in Tirora in Gondia district of Maharashtra, India. He received his bachelor degree in Pharmacy from Nagpur University, India with Gold Medal in **2009**. He qualified GATE exam and awarded fellowship to pursue M.S. Pharm. from NIPER Hyderabad, India in 2011. After two years of industrial/academic experience **(2011-2013)**, he joined Prof. P. V. Bharatam laboratory at NIPER Mohali in **2013** to pursue doctorate degree (Ph.D.). He also visited a group of Prof. Beifuss at University of Hohenheim, Stuttgart, Germany for a peri-

od of **2 months (Feb-March 2018)**. His research interest during PhD includes study on the structural properties of interesting organic compounds and their application in medicinal chemistry, organic chemistry and pharmaceutical sciences. He was awarded with doctor of philosophy degree (Ph.D.) in **2019**. Dr. Sumit is currently working as a group leader at IOL Chemicals and Pharmaceuticals Ltd, Punjab, India. As a group leader his role is to develop an efficient, scalable and sustainable green process for the synthesis of active pharmaceutical ingredients (API) free from genotoxic impurities.

Exploration of Cultivable Actinomycetes in Producing Extracellular Enzymes and their Therapeutic Applications

Jayachandra S. Y.[1,2], M. H. Kontro[2] and **Dayanand A.[1]**

[1]Department of Biotechnology, Basaveshwar Engineering College, India
[2]Department of Environmental Sciences, University of Helsinki, Finland
[3]Department of Microbiology, Gulbarga University, India

Actinomycetes have been studied thoroughly in respect to their community structures and distribution, as they possess realistic and ecologically important metabolites and produce many industrially sustainable products. Due to their rapid metabolic rates and accumulation of various bioactive compounds, they are being extensively used for environmental and biotechnological applications. Many of the produced antibiotics are mainly derived from actinomycetes. It is always vital to investigate the cultivable communities of actinomycetes over uncultured or uncultivable groups because of their growth in the artificial media and thus controlled transformation substrates into useful products. But, designing media for cultivating the novel groups of actinomycetes has always been an enormous challenge, which could lead to the novel metabolites discovery. In exploring such microbes, conducted extensive research work on recent trend in Actinobacteria diversity of environment and their bioactive molecules. As a part of the research objectives various samples like ground water sediment, compost and garden soil samples were used to screen the potential strains, 40 strains were recovered upon grown them on different substrates such as cellulose, hemicellulose, lignin and tyrosine, identified as a potential producers of industrially important enzymes like Cellulase, Ligninase, Hemicellulase and L-Tyrosinase enzymes. Multiple enzymes producing capability of each strain were analyzed. Then the qPCR technique was carried out to amplify the DNA content of each individual strain and 16S rRNA gene sequencing was carried out in identification of the strains, classification and community structures were studied. After this extensive investigation we are keen to understand how these extracellular enzymes are expressed in compost derived and what are their functions especially their use in treatment of various cancers, cardiovascular disorders and also can help in development of novel drug delivery systems.

Biography

Dr. Jayachandra S. Yaradoddi is presently working as an Assistant Professor, Department of Biotechnology, Basaveshwar Engineering College, Bagalkote, Karnataka, India. Obtained his Master's and Doctoral degree from the Gulbarga University, Kalaburagi. He has fifteen years of Research and Teaching experience. Received research grants from various funding agencies. Received grant from the prestigious Päijät-Hämeen Rahasto, Finland to do his Postdoctoral Research in the University of Helsinki, Niemenkatu, Lahti, Finland under the supervision of Prof. Merja H. Kontro. Co-guided one Ph.D. and supervised 20 undergraduate projects. He has received the prestigious "AORP" from the VGST, GoK. Published more than 70 peer reviewed articles in various national and international journals of repute and filed an Indian patent, Authored 3 Books. Fellow member and member in various scientific societies. He is recognized as reviewer for various peer reviewed international standard journals and also Editorial member of Research Journal of Biotechnology.

Early-Stage Detection of Furcation Radiolucency in Primary Mandibular Molars using Vision Transformer

Naveen Aggarwal[1], Manoj Kumar Jaiswal[2] and **Mamta Juneja[1]**

[1]UIET, Panjab University, India,
[2]Oral Health Sciences Centre, PGIMER, India

Early childhood caries (ECC) is a prevalent oral health issue globally, affecting infants and preschoolers. Its severity can lead to furcation involvement in primary molars, a critical dental concern. Furcation radiolucency, a dark shadow between tooth roots on X-rays, indicates bone loss in this region as shown in Figure 1. Its early detection is crucial for timely intervention, preventing tooth extraction. Studies till date have not focused on pediatric IOPA for diagnosis of furcational pathology. The present study aims to apply a deep learning based architecture for effective pre-processing of periapical radiograph followed by improved segmentation and classification to detect furcation radiolucency in primary mandibular molars. For effective training and validation of models, we have created a labelled dataset of 5000 images from Retrospective cohort data of IOPA images taken from the Oral Health Sciences Centre, PGIMER Chandigarh INDIA. At the time of screening, the images with region of interest are manually cropped and further divided into two groups for model training.

The detection stage utilizes Faster-RCNN to accurately identify deciduous teeth and areas of furcation involvement. Performance is further enhanced by a novel ensemble-based Deciduous Detection Boosting (DDB) technique. For effective classification of furcation areas, we propose a spatial attention-based Vision Transformer (ViT) that processes resized segmented areas. The model is trained over multiple epochs to optimize parameters, then fine-tuned with hyper parameter adjustments on a validation set. Figure 2 represents the performance of proposed model trained over multiple epochs achieving an accuracy of 98.91%. This study could significantly aid in the early detection of furcation radiolucency in primary mandibular molars using IOPA radiograph images. A web interface for visual representation of detectable furcation lesions is also designed to assists doctors in treatment planning and report generation.

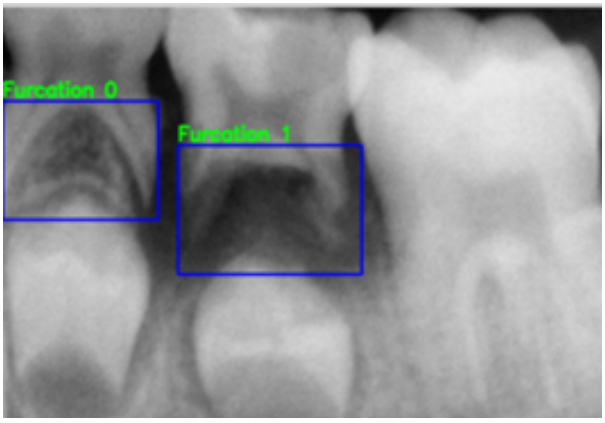


Figure 1: Deciduous teeth and the region of interest for furcation defects.

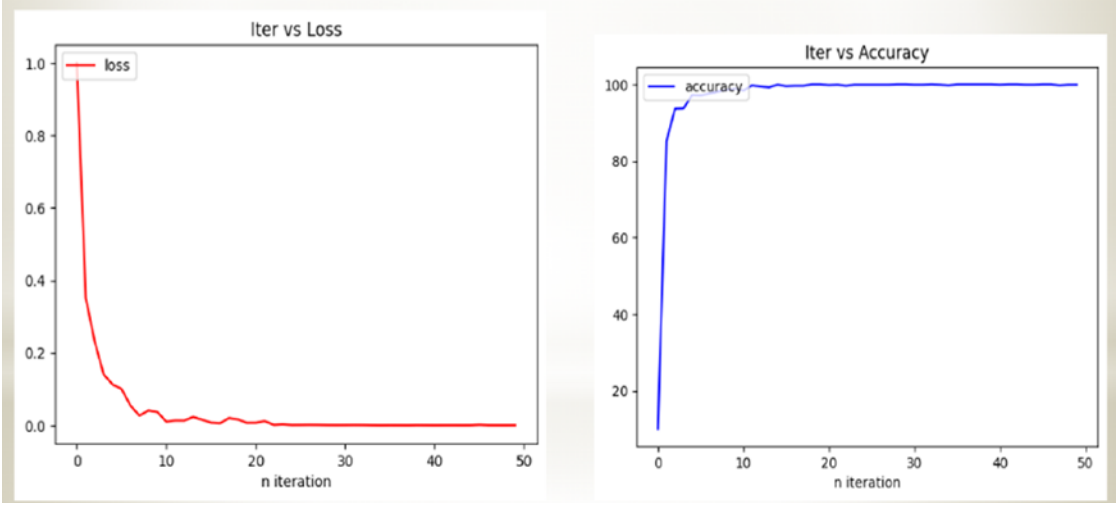


Figure 2: Performance of ViT on IOPA Dataset.

Biography

Naveen Aggarwal is working as a Professor in UIET, Panjab University, INDIA and has more than 22 years of teaching experience. He is currently In Charge of Panjab University Incubation Centre and Project Coordinator in Design innovation Centre established by Ministry of Education, Government of INDIA. He has more than 175 publications and 2 patents are granted to him. He has completed more than 15 research funded project and 4 software consultancy projects. He is Senior Member of ACM & IEEE.

Triclosan-Induced Histopathological Alterations, Oxidative Stress and Immune Dysfunction in The Skin of The Fish, *Cyprinus carpio*

Usha Kumai[1], Anchal Tripathi[1], Tuhina Gayen[1] and **Swati Mittal[2]**

[1]Zoology Section, Mahila Mahavidyalaya, Banaras Hindu University, India
[2]Department of Zoology, Institute of Science, Banaras Hindu University, India

Triclosan (TCS), a widely used broad-spectrum antibacterial agent in several personal care and household products, is found in various aquatic environments at concentrations capable of causing detrimental effects to non-target organisms. Due to high lipophilicity, it can also be easily absorbed through the body surface of aquatic organisms. The study investigated the impact of three sublethal concentrations (1 µg/L, 10 µg/L and 100 µg/L) of TCS on the skin of fish *Cyprinus carpio* for 28 days. The histopathological alterations observed in the skin epidermis were hypertrophy, hyperplasia, and sloughing of epithelial cells. Intracellular vacuolisation, shrinkage, and degeneration in the content of club cells were also observed. The results of the biochemical analysis showed a significant ($p<0.05$) decrease in the activity of superoxide dismutase, catalase, glutathione-s-transferase, glutathione reductase, glutathione peroxidase, and reduced glutathione content. However, a significant ($p<0.05$) increase in the activity of acid phosphatase, alkaline phosphatase, lactate dehydrogenase; and the level of lipid peroxidation and nitric oxide was observed in the exposed groups till 28 d. In addition, TCS inhibited acetylcholinesterase activity from 7-28 d while significant accumulation in acetylcholine content was observed at the end of 28 d. A significant concentration-dependent increase in glucose, triglyceride, cholesterol and cortisol levels was observed at 28 d of exposure. Moreover, TCS exposure increased IL-6, TNF-α, and a decline in IL-10 at 28 d of exposure duration. This study reveals that TCS exposure alters the fish skin physiology affecting its barrier function.

Biography

Dr. Usha kumari is currently working as Assistant Professor in Zoology at Mahila Mahavidyalaya, Banaras Hindu University. Her area of research is fish biology and aquatic toxicology. Her research interests include understanding adaptive modifications in different groups of fishes in relation to their habit and habitat and the impact of emerging pollutants on fish physiology. She has received several awards and published more than forty research articles in peer-reviewed international journals.

Acoustic Wave-Enhanced Disruption of Cellular Membranes: Implications for Medicinal Chemistry and Diagnostics

Sushama Agarwalla, Sunil Kumar Singh and **Suhanya Duraiswamy**

Indian Institute of Technology Hyderabad, India

We present a novel microfluidic approach for rapid and efficient cell lysis, leveraging traveling surface acoustic waves (TSAWs) to extract nucleic acids and proteins from various biological samples. Our design utilizes TSAWs generated by interdigitated transducers on a piezoelectric substrate to disrupt cellular membranes within a microfluidic channel. Through numerical simulations and experimental validation, we optimized the TSAW parameters to achieve high lysis efficiency (>95%) for bacterial cells within seconds, using low voltage and frequency. Our method outperforms traditional lysis techniques, offering a fast, efficient, and amplifier-free solution for lysing diverse biological samples. This innovative TSAW-based microfluidic cell lysis strategy has potential for integration with nucleic acid-based diagnostics and point-of-care devices, enabling rapid and accurate analysis of biological samples.

Biography

Sushama Agarwalla is a PhD research scholar in the MuRE Laboratory, guided by Dr. Suhanya Duraiswamy. Her research focuses on infectious disease diagnosis, specifically developing rapid diagnostic tools. They have developed "Sepsikit," a novel kit that isolates and detects pathogens within 1.5 hours. This innovation aims to revolutionize sepsis diagnosis and treatment. Through their research, they strive to develop cutting-edge diagnostic technologies that improve healthcare outcomes and save lives, addressing the urgent need for rapid and accurate infectious disease diagnosis.

Antimicrobial Potential of *Potentilla indica* (Andrews) Th. Wolf Extracts against ESKAPE Pathogens and *Candida albicans*: A Step Towards Combating Antimicrobial Resistance

Dimple Guleria, Shikha Dhiman, Priyanka Sharma and **Amit Kumar Sehgal**

Department of Bio-Sciences, Himachal Pradesh University, India

Antimicrobial resistance (AMR) is an escalating global health challenge, particularly against pathogens categorized as ESKAPE by the World Health Organization (WHO). This study explores the antimicrobial potential of *Potentilla indica* (Andrews) Th. Wolf, a wild berry native to the Himalayas, traditionally used in local medicine, against major bacterial and fungal pathogens. The tested microorganisms included *Escherichia coli, Staphylococcus aureus, Streptococcus mutans, Streptococcus pneumoniae, Klebsiella pneumoniae, Pseudomonas aeruginosa* (ESKAPE pathogens) and *Candida albicans*. Acetone and methanol extracts of the aerial parts of *P. indica* were evaluated using the disk diffusion method and minimum inhibitory concentration (MIC) assays. The acetone extract exhibited remarkable antibacterial activity, with the largest zone of inhibition (31.89 ± 0.05 mm) observed against *P. aeruginosa*. Conversely, the methanol extract showed superior antifungal activity, achieving a significant zone of inhibition (11.90 ± 0.33 mm) against *C. albicans*. MIC assays further revealed that both extracts displayed the lowest MIC value (39.1 µg/mL) against *S. mutans,* followed by substantial activity against *S. pneumoniae, P. aeruginosa* and *C. albicans* at 1250 µg/mL. These findings highlight the promising antimicrobial properties of *P. indica* extracts, with the acetone extract showing particular effectiveness against bacterial pathogens and the methanol extract demonstrating efficacy against fungal infections. This study supports the traditional medicinal use of *P. indica* and underscores its potential as a source for developing novel antimicrobial agents to address the growing threat of AMR.

Biography

Dimple Guleria is a PhD research scholar at Himachal Pradesh University, Shimla. Her research converges on the pharmacological and nanotechnological potential of medicinal plants, integrating traditional knowledge with modern scientific methodologies. Her MPhil research on *Jatropha curcas* L. yielded two publications and she has qualified for prestigious national fellowships in India (CSIR-NET JRF and GATE). Her research aims to develop innovative, sustainable plant-based solutions for global health challenges.

Nrf2 a Novel Target of Cancer Treatment

Muhammad Haidar Zaman[1], Jiayi Gong[2] and **Ashfaq Ahmad Shah Bukhari[3]**

[1]Department of Health and Biological Sciences, Abasyn University, Pakistan
[2]Faculty of Science, University of Hong Kong, China
[3]Department of Physiology, RAK Medical and Health Sciences University, UAE

The cross-talk between cancer-associated fibroblasts (CAFs) and cancer cells in the tumor microenvironment (TME) facilitates tumor development, especially regarding tumor initiation and metastasis, and confers chemoresistance. Nrf2 is a transcription factor that can prevent the cell from oxidative stress and regulate the metabolizing pathway through promoted transcription of cytoprotective antioxidant genes. Its abnormal activity has been reported in plenty of cancers including colorectal cancer (CRC). However, what role Nrf2 plays in colorectal CAFs has not been determined. In this study, we confirmed that the colorectal CAFs isolated from murine CRC tissues have a high level of Nrf2 which is highly expressed in murine colon carcinoma cell CT26. To study the role of Nrf2 IN colorectal CAFs, we screened out the concentration and time of Nrf2 inhibitor, ML385 which could have the maximum inhibition of Nrf2 in CAFs. Down-regulated Nrf2 by ML385 significantly affected proliferation and prevented migration in colorectal CAFs, but does not influence cell survival and apoptosis. Besides, the down-regulation of Nrf2 in CAFs can reduce the proliferation and stemness of the CRC cells co-cultured with CAFs *in vitro*. In summary, the Nrf2 antagonist, ML385 can reduce cell proliferation and migrations in colorectal CAFs, and decrease cell proliferation and stemness of CRC cells co-cultured with CAFs. It is hypothesized that the regulation of Nrf2 in CAFs may become a new target of treatments for CRC.

Biography

Dr. Muhammad Haidar Zaman is an Associate Professor in Immunology, at the *Department of Health and Biological Sciences, Abasyn University Peshawar, Pakistan* and also works in Nan Shi Fu Zhong school of Nanjing Normal University. He earned his Ph.D in immunology from *Nanjing Medical University, China* and a Postdoc in Immunology from *Jiangsu Centre for Disease Control and Prevention (CDC), China.* He is a member of the *American Society for Microbiology (ASM)*, and a former member of the *European Academy of Allergy and Clinical Immunology (EAACI).*

Impact of Green Pathways on Memory and Cognition: Identification of Potential Therapeutic Agents for Alzheimer's Disease to Improve Mental Health

Mehreen Lateef[1], Laraib Liaquat[1], Sehar Khan[2] and **Saima Saleem[2]**

[1]Bahria University College of Allied Health Sciences, Bahria University Health Sciences Campus Karachi, Pakistan

[2]Dr A.Q Khan Institute of Biotechnology and Genetic Engineering, University of Karachi, Pakistan

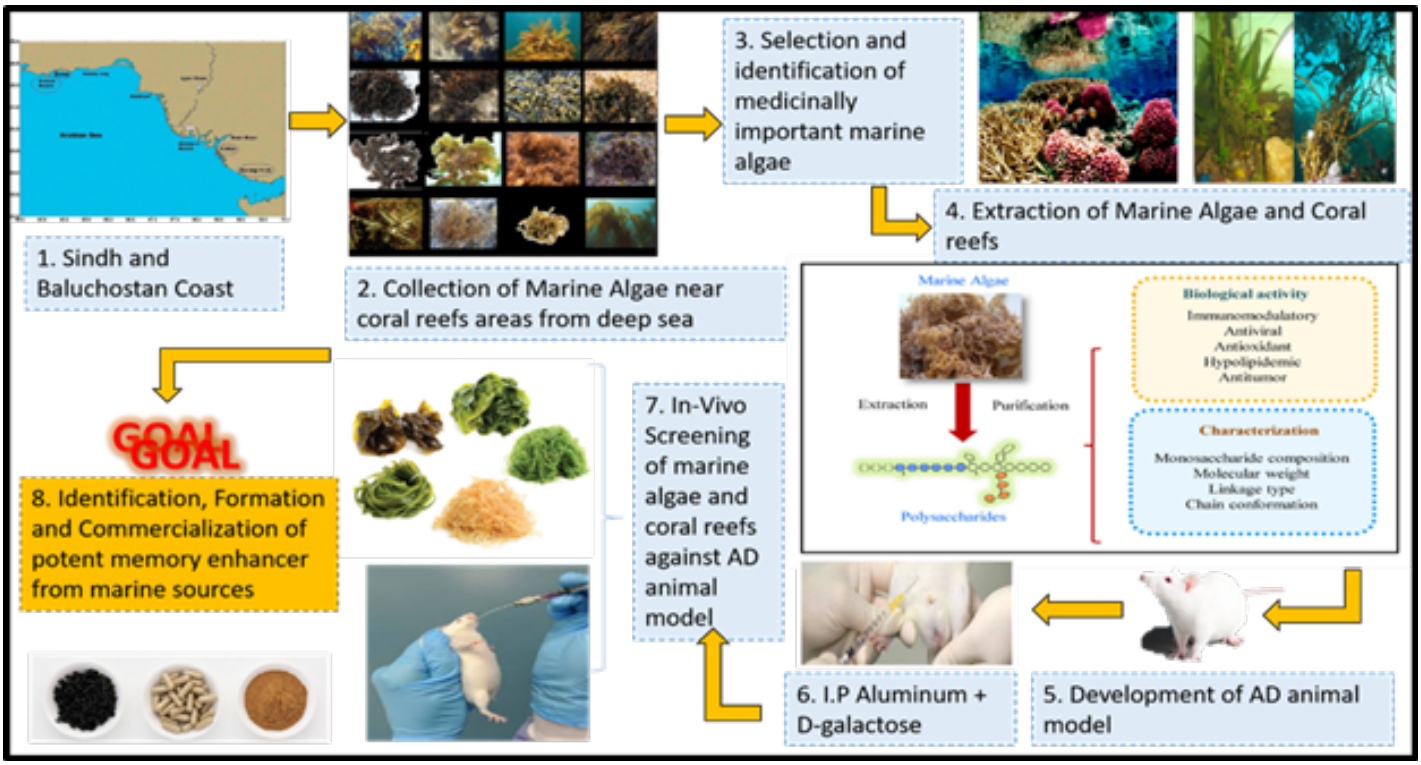
Introduction: Pakistan is a lower-middle income country with an estimated one million people living with dementia. The most common type of dementia includes Alzheimer's disease (AD) which accounts for 50–75% of all cases of old age. AD related dementia is also becoming a serious health issue in Pakistan and due to lack of awareness, its incidence and progression is increasing gradually rapidly. As there is, no treatment available for such dementia related problems. Therefore, there is an intense need of development of therapeutic strategy that cannot only improve brain functions but can also prevent developing neurodegeneration.

Objectives: This is study is focused isolation of unexplored marine flora and fauna of Pakistan by exploring their neuroprotective effects through *in vitro* and *in vivo* studies studies. Genetic analysis based on the single nucleotide polymorphism(s) in the B-cell lymphoma2 gene (BCl-2) (rs921884063) with susceptibility to AD was also studied in human population.

Methods: Various seaweeds were collected from Karachi coast. After specie identification of marine algae, isolated extracts were tested for Acetyl cholinesterase (AChE) and butrylcholinesterase inhibition *in vitro* assays by ELISA technique. Behavioral, Biochemical, Histopathological analyses were also performed. In human analysis, genomic DNA was extracted through the salting-out method. Targeted polymorphism(s) was amplified through Tetra-primer Amplified Refractory Mutation System Polymerase Chain Reaction (T-ARMS PCR) for age matched healthy controls and AD patients

Results: Results showed that pre-treatment significantly protected AD-like behavioral disturbances in rats with marked memory decline was observed in AD model rats along with significant oxidative stress. Genetic studies in humans revealed that the (rs921884063) polymorphism in BCl-2 was significantly associated with risk (OR>1, p<0.01) in the progression of AD.

Conclusion: This study showed the therapeutic potential of sea weeds by enhancing neuroprotective and cognition function through preclinical trials for its future application to manage Alzheimer's disease.



Biography

Professor Dr. Lateef is currently serving as Principal of Bahria University College of Allied Health Sciences and head of Multidisciplinary Research Lab in Bahria University Health Sciences Campus. She did her PhD in Biochemistry from University of Karachi in collaboration with Heritage College of Osteopathic Medicine, Ohio University, USA. She was associated 10 years with Pharmaceutical Research Centre of Pakistan Council of Scientific and Industrial Research Complex Karachi. She has research experience in the field of Enzymology and Clinical Biochemistry for the last 20 years. Her expertise is based on Enzyme Inhibition Studies of Phyto pharmaceuticals and Synthetic Lead Compounds against various diseases. She is currently involved in research projects on analysis of genetic and serum biomarkers related to osteoporosis, Alzheimer's disease and diabetic foot ulcer with ongoing research projects on marine bioprospecting. She has total of 137 international publications a with 3 national patents at her credit.

A Randomized, Double-blind, Placeo-Controlled Trial Assessing the Efficacy and Safety of a Fixed-Dose Combination (FDC) of MEtformin Hydrochloride 1000 mg ER, SItagliptin Phosphate 100 mg, and DApagliflozin Propanediol 10 mg in Indian Adults with Type 2 Diabetes: The MESIDA Trial

Akhilesh Sharma[1], Mayur Mayabhate[1], Awadhesh Kumar Singh[2], Rakesh Sahay[3] and **Navneet Gill[4]**

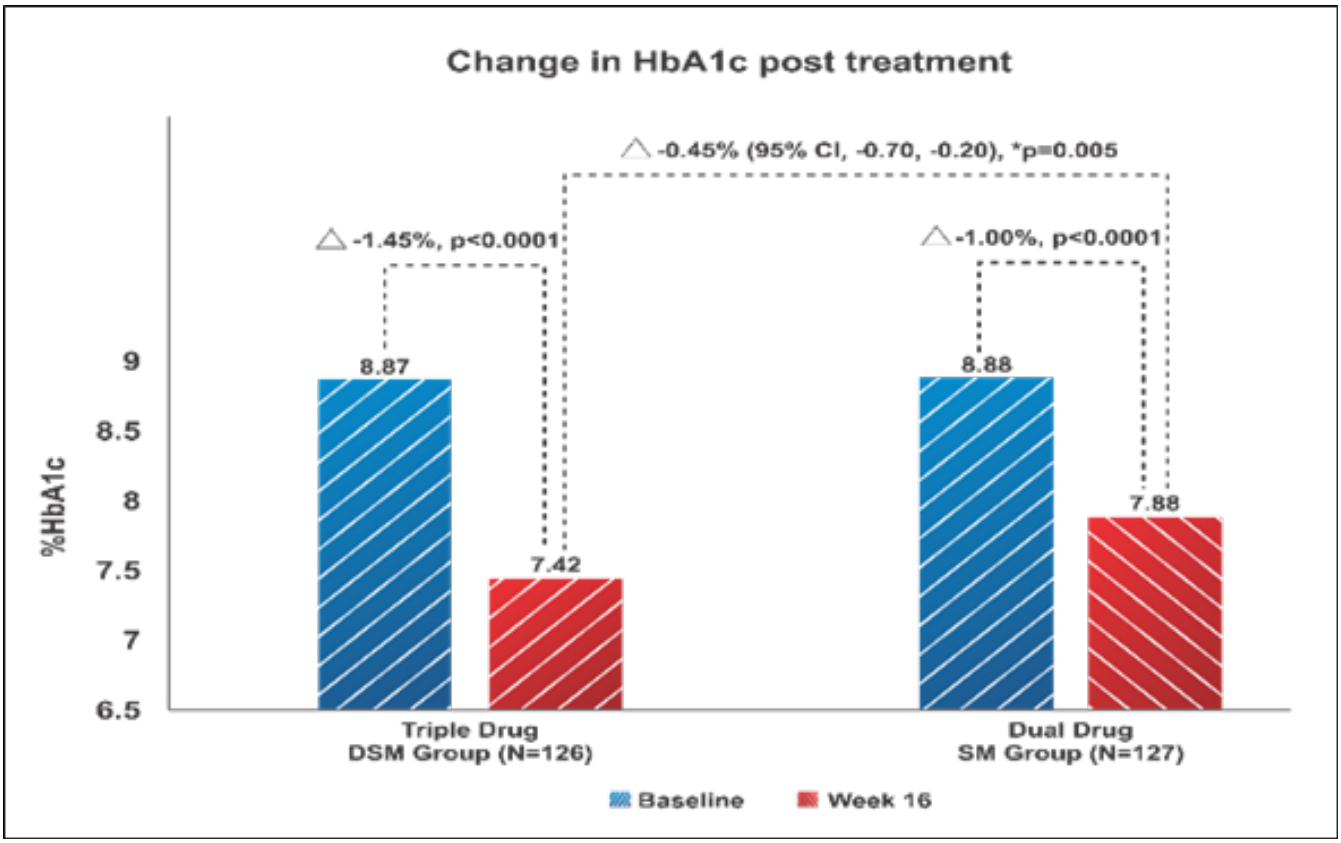
[1]Medical Affairs, Alkem Laboratories Mumbai
[2]G. D. Hospital & Diabetes Institute, India
[3]Osmania Medical College, India
[4]Aakash Healthcare Pvt. Ltd. Hospital, India

Background and Aims: To assess the efficacy and safety of fixed-dose combinations (FDC) of triple-drug dapagliflozin, sitagliptin, and metformin (DSM) compared with FDC of two-drug sitagliptin and metformin (SM), in Indian adult patients with type 2 diabetes (T2D).

Methods: A multicentric, randomized, double-blind, active-controlled, Phase 3 study (CTRI/2021/10/037461) was conducted on 274 Indian adult patients with T2D. Patients were randomized (1:1) to receive either an FDC of triple-drug (n = 137) dapagliflozin propanediol 10 mg, sitagliptin phosphate 100 mg, and metformin hydrochloride 1000 mg extended-release (DSM) or FDC of two-drug (n = 137) sitagliptin phosphate 100 mg and metformin hydrochloride 1000 mg sustained-release (SM), for 16 weeks. The primary endpoint was a change in HbA1c, while the secondary endpoints were changes in fasting plasma glucose (FPG), postprandial glucose (PPG), body weight, and safety.

Results: Both DSM and SM FDCs reduced HbA1c significantly (-1.45% and -1.00%, respectively, both P < 0.0001), however, HbA1c lowering was superior with DSM (Δ -0.45%; P = 0.0005) compared to SM, at week 16. Similarly, both DSM and SM FDCs reduced FPG and PPG significantly, however, FPG (Δ -12.4 mg/dl; P = 0.003) and PPG reduction (Δ -18.45 mg/dl; P = 0.01) were significantly superior to DSM compared to SM, respectively. No significant reduction in body weight was observed between the two arms. Both FDCs were well tolerated.

Conclusion: FDC of DSM was superior to SM in reducing HbA1c, FPG, and PPG in Indian adults with T2D. Both triple and dual FDCs had optimal safety profiles.



HbA1c change at Week 16 from baseline. Abbreviations: HbA1c: haemoglobin A1c; SM: Sitagliptin 100 mg + Metformin 1000 mg sustained release; DSM: Dapagliflozin 10 mg + Sitagliptin100 mg + Metformin 1000 mg extended release.

Biography

Dr. Akhilesh Sharma- M.D. from Mumbai, Fellow of Royal Liverpool hospital society-U.K, advanced training in Clinical Research at Berkley Extension, California State University, USA and Global Pharmacovigilance, Luton Medical Centre, UK. Has around 30 years of worldwide experience in areas of Clinical Research, Medical Affairs, Market Access, Regulatory, Pharmacovigilance, Translation Medicine, Biomarkers, Clinical Pharmacology across various multinational pharmaceutical companies, based at US & India.

Currently President & Chief Medical Officer for Alkem Laboratories Ltd.

Also, co-founded biomarker research organization GeneXY in Philadelphia, USA jointly with Wistar institute, Pennsylvania university campus.

Advisor to special projects at Harvard-Wyss, visiting faculty at Texas Tech University- Innovation hub (USA). Been on panel of Drug Development, Clinical Research and Drug Safety at various national and international forums including at USFDA workshops and an invited faculty at leading international conferences & institutes. Passionate about translational research and innovations in drug developments and clinical trials.

Has to credit more than 58 scientific & research publications, 52 patents and holds membership of International Pharmaceutical Society, American Academy of Dermatology, American Diabetes Association, European Society of Respiratory Medicine.

Assessment of The Antileishmanial Activity of Diallyl Sulfide Combined with Meglumine Antimoniate on *Leishmania major*: Molecular docking *in vitro* and Animal model

Farzaneh Zarrinkar and **Iraj Sharifi**

Leishmaniasis Research Centre, Kerman University of Medical Sciences, Iran

Currently, no safe vaccine against leishmaniasis is available. So far, different control strategies against numerous reservoir hosts and biological vectors have not been environment friendly and feasible. Hence, employing medicinal components and conventional drugs could be a promising approach to developing novel therapeutic alternatives. This study aimed to explore diallyl sulfide (DAS), a dynamic constituent of garlic, alone and in a mixture with meglumine antimoniate (MAT as standard drug) using *in vitro* and animal model experiments against Leishmania major stages. The binding affinity of DAS and four major defence elements of the immune system (iNOS, IFN-γ, IL-12, and TNF-α) was used to predict the predominant binding mode for molecular docking configurations. Herein, we conducted a broad range of experiments to monitor and assess DAS and MAT potential treatment outcomes. DAS, combined with MAT, displayed no cytotoxicity and employed a powerful antileishmanial activity, notably against the clinical stage. The function mechanism involved immunomodulation through the induction of Th1 cytokine phenotypes, triggering a high apoptotic profile, reactive oxygen species (ROS) production, and antioxidant enzymes. This combination significantly decreased cutaneous lesion diameter and parasite load in BALB/c mice. The histopathological findings performed the infiltration of inflammatory cells associated with T-lymphocytes, particularly CD4+ phenotypes, as determined by biochemical markers in alleviating the amastigote stage and improving the pathological changes in *L. major* infected BALB/c mice. Therefore, DAS and MAT deserve further advanced therapeutic development and should be considered as possible candidates for treating volunteer cases with cutaneous leishmaniasis in designing an upcoming clinical trial.

Biography

Farzaneh Zarrinkar was born on 21 September 1974 in Tabriz, Iran. She completed her primary to high school education in the same city, graduated from Nobovat High School in 1992. After moving to the Netherlands with her spouse in 1992, she earned NT2 Dutch language certificate in 1995 and MHLE English language certificate in 2015. She enrolled in Laboratory Sciences at Highschool Rotterdam and Suburbs, but returned to Iran in 1997 due to her spouse's PhD completion. She continued her studies at Tehran University of Medical Sciences, obtained an associate degree in Laboratory Sciences in 1999. Then she earned a Bachelor's degree in Medical Entomology and Vector Control from Tehran University in 2002, and a Master's degree from Tabriz University of Medical Sciences in 2012. After working at the Pasteur Institute of Iran, she pursued a PhD at Kerman University of Medical Sciences, completed it in 2024 with two research papers.

Novel Effect of Topical Roquinimex and Its Combination with Clobetasol on an Imiquimod-Induced Model of Psoriasis in Mice

Abeer Mohammed Hasan[1] and **Fouad Kadhim Gatea**[2]

[1]Department of Pharmacology, College of Pharmacy, Uruk University, Iraq
[2]Department of Pharmacology and Therapeutics, College of Medicine, Al-Nahrain University, Iraq

Psoriasis is a chronic inflammatory skin condition affecting multiple systems and the skin, with topical therapy representing the fundamental treatment modality for psoriasis. Investigate the effect of topical Roquinimex (ROQ) alone and combined with Clobetasol propionate (CLO) on imiquimod (IMQ)-induced mouse model as a novel approach to treating psoriasis. Sixty male Swiss Albino mice were divided into six groups of ten mice; all groups except the negative control received IMQ cream 5% (62.5 mg) as a once-daily topical application for six days. On the seventh day, five groups (except negative control) received one of the following treatments for eight days: no treatment (positive control), Petrolatum gel 15% as a twice-daily topical application (Petrolatum control), CLO 0.05% ointment once daily, ROQ ointment 1% w/w twice daily topically, topical preparation of 0.025% CLO ointment combined with ROQ ointment 0.5% w/w twice daily; the total duration of the study is 14 days. The clinical, pathological, and laboratory effects were then measured. The use of ROQ ointment alone or combined with CLO resulted in significant improvement in psoriasis lesions (measured by Baker's and PASI scores) compared to positive control groups (2.15±1.08, 1.60±0.61, 9.00±0.00, and 7.60±0.84, respectively for Baker's score) (1.50±1.08, 1.30±0.95, 11.70±0.48, 9.30±0.67, respectively for PASI score), a similar improvement seen for various inflammatory markers, including interleukin (IL)-10 (140.53±60.68, 285.63±92.16, 31.83±3.03, and 92.50±27.13 pg/ml, respectively), IL-17 (126.58±40.98, 124.26±61.40, 553.04±141.32, and 278.52±100.27 pg/ml, respectively), tumor necrosis factor-α (72.34±23.40, 30.11±7.01, 807.13±500.06, and 281.79±240.17 pg/ml, respectively), and vascular endothelial growth factor (109.71±29.35, 80.96±24.58, 552.20±136.63, 209.56±73.31 pg/ml and respectively). Roquinimex exerts its antipsoriatic effect through multiple mechanisms; its combination treatment with Clobetasol is a promising therapy for managing psoriasis.

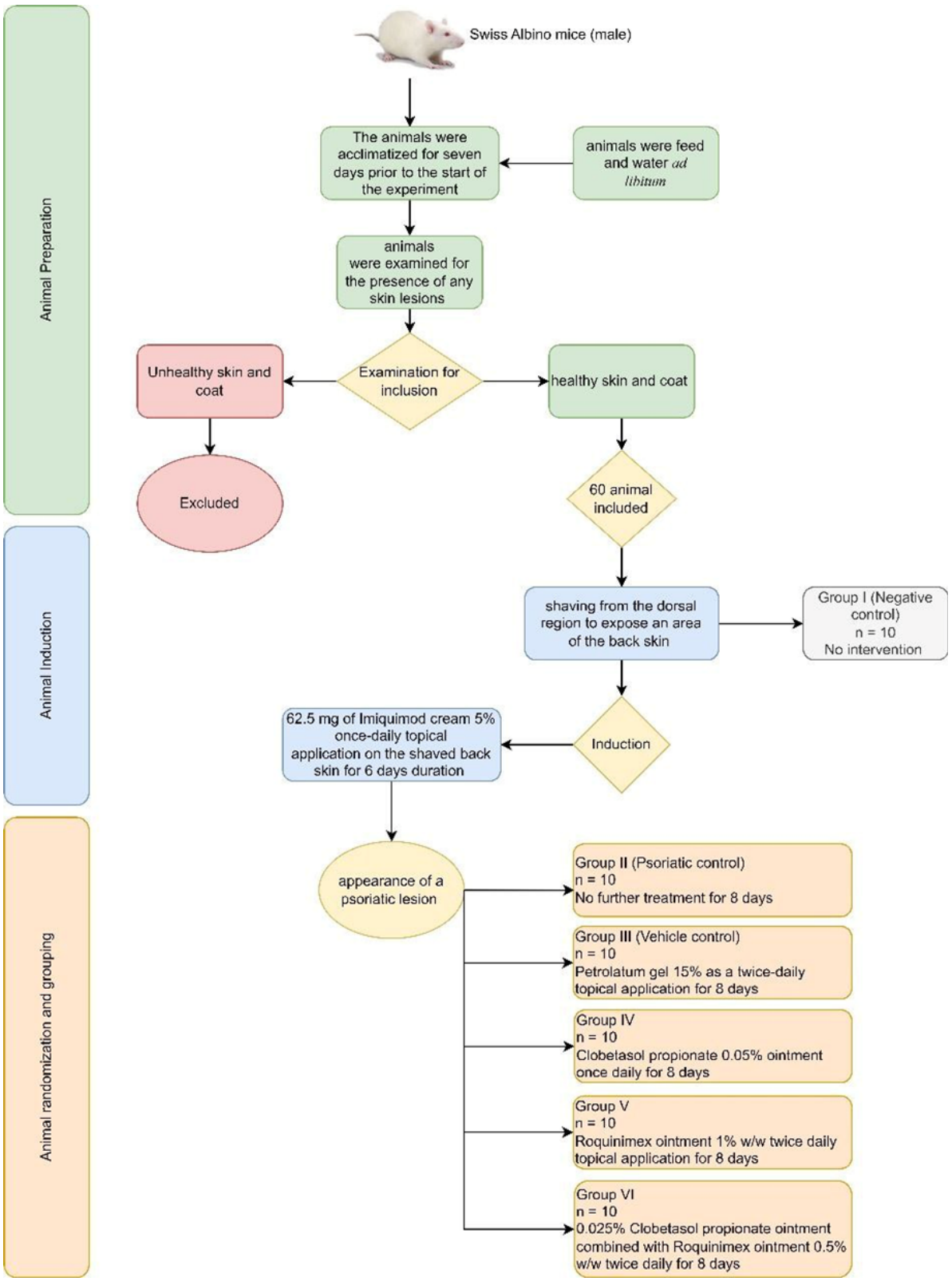


Fig. 1 Flow chart of the study

Table 1: Assessment of histopathological examination

Parameters	Baker's score	PASI score
Group I	-	-
Group II	9.00±0.00[a]	11.70±0.48[a]
Group III	7.60±0.84[b]	9.30±0.67[b]
Group IV	2.15±1.08[c]	3.00±0.82[c]
Group V	1.60±0.61c[d]	1.50±1.08[d]
Group VI	1.05±0.28[d]	1.30±0.95[d]
p-value	<0.001***#	<0.001***#

p-value Columns with similar letters indicate no significant difference (p-value >0.05), while different litters indicate a significant difference (p-value≤0.05)
One Way ANOVA (Post hoc Tukey test)
*** indicates a highly significant difference
SD: standard deviation, PSAI: psoriasis area and severity index

Table 2: Assessment of biomarkers

Parameters	IL-10 (pg/mL)	IL-17 (pg/mL)	TNF-a (pg/mL)	VEGF (pg/mL)
Group I	286.26±63.80[a]	222.41±64.33[bc]	83.46±6.02[b]	120.99±15.83[bc]
Group II	31.83±3.03[c]	553.04±141.32[a]	807.13±500.06[a]	552.20±136.63[a]
Group III	92.50±27.13[bc]	278.52±100.27[b]	281.79±240.17[b]	209.56±73.31[b]
Group IV	168.11±57.07[b]	165.07±43.59[c]	65.37±23.12[b]	134.57±44.28[bc]
Group V	140.53±60.68[b]	126.58±40.98[c]	72.34±23.40[b]	109.71±29.35[c]
Group VI	285.63±92.16[a]	124.26±61.40[c]	30.11±7.01[b]	80.96±24.58[c]
p-value	<0.001***#	<0.001***#	<0.001***#	<0.001***#

Columns with similar letters indicate no significant difference (p-value >0.05), while different litters indicate a significant difference (p-value≤0.05)
One Way ANOVA (Post hoc Tukey test)
*** indicates a highly significant difference
SD: standard deviation, IL= Interleukin; TNF-a= Tumor necrosis factor alpha; VEGF=Vascular endothelial growth factor

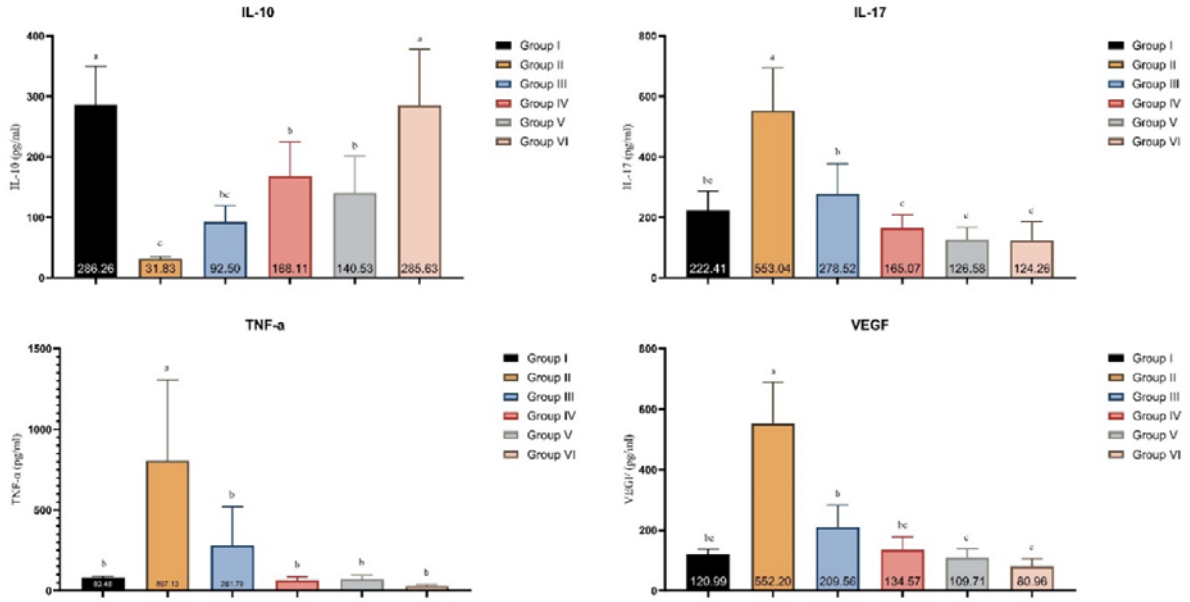


Fig. 2 Histogram of biomarkers

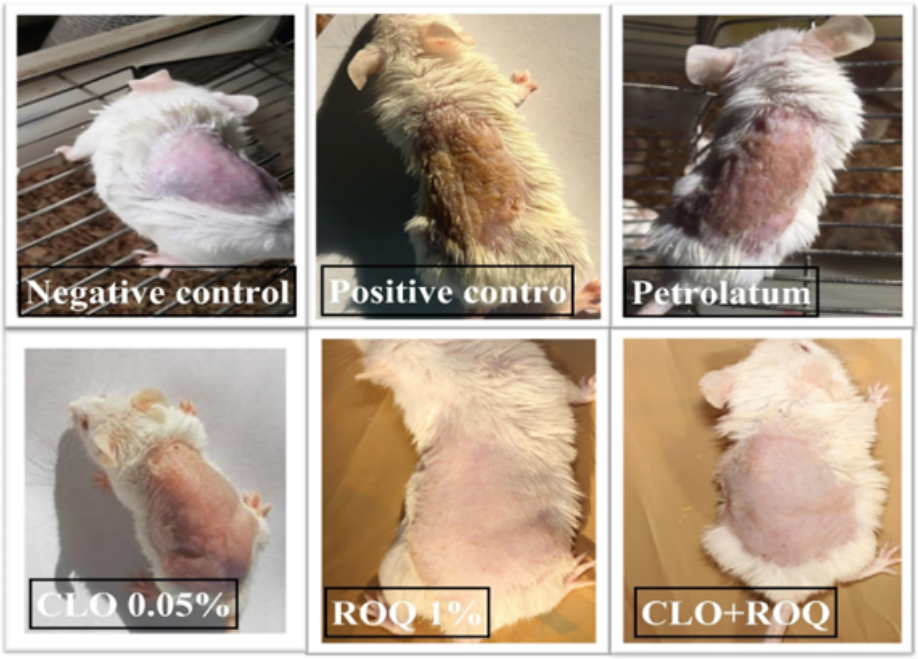


Figure 3: Effect of tested agents on the severity of a psoriasiform skin lesion. Negative control; Positive control (Imiquimod 5%); Petrolatum; CLO, clobetasol; ROQ, roquinimex; CLO+ROQ clobetasol plus roquinimex.

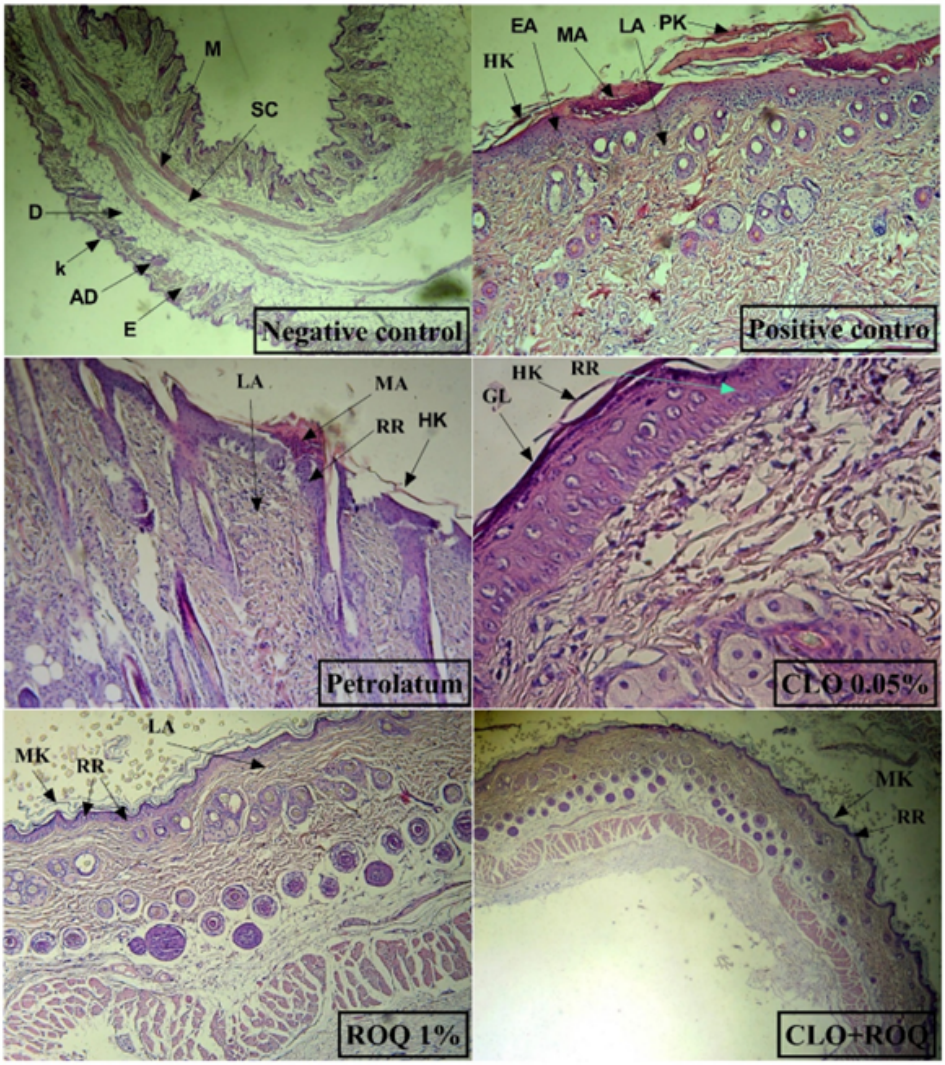


Fig. 4 Hematoxylin and eosin–stained histopathological skin sections from groups of mice at 40X/10X.magnification: Negative control group showed the normal keratin layer (K), the normal epidermis (E), the normal dermis (D), the subcutaneous tissue (SC), and the muscular layer (M). Positive control group and Petrolatum showed hyperkeratosis (HK), parakeratosis (PK), dense neutrophilic infiltration (Munro's abscess [MA]), epidermal acanthosis (EA), thinning papillae and rete ridges (RR), and lack of granular layer (GL) the dermis has moderate to severe inflammatory lymphocytic infiltration (LA). Mice in the CLO 0.05% group showed hyperkeratosis (HK), absence of (parakeratosis (PK) and Munro's abscess (MA)), presence of epidermal granular layer (GL) with minor acanthosis (EA), papillary thinning and few rete ridges (RR), the dermis has mild lymphocytic infiltration (LA). Mice treated with ROQ 1% showed minor keratosis (MK) with no Munro's abscess (MA) no parakeratosis (PK), mild acanthosis (MA), and few rete ridges (RR). (CLO+ROQ) group showed modest keratosis with no Munro's abscess (MA) and no parakeratosis (PK)

Biography

Abeer Mohammed Hasan Garma, MSc in Pharmacology (2024), is a Specialist Pharmacist at Uruk University, with a distinguished background in clinical pharmacology, education, and research. She holds a Master's in Pharmacology from Al-Nahrain University College of Medicine and graduated from the College of Pharmacy, Baghdad University, in 2012. Abeer's clinical expertise has been honed through her roles at key institutions, including Al-Kindy Hospital, Al-Alwiya Maternity Hospital, and Imam Ali Hospital. At Ibn Al-Balady Hospital, she led pharmacovigilance initiatives, enhancing drug safety, and at Alwiya Children's Hospital, she directed continuing education programs for pharmacists while overseeing training for newly appointed staff.

Abeer is also known for engaging lectures in pharmacology and toxicology, inspiring healthcare professionals with her insights. Her innovative research, published in *Naunyn-Schmiedeberg's Archives of Pharmacology* (Springer Nature), reflects her commitment to advancing pharmacological therapies and innovative products. She is honoured to be a distinguished speaker at the 6th Global Summit on Advances in Medicinal Chemistry and Pharmacology" (Adv. Med Chem 2025).

Sodium Citrate Buffer Improves Pazopanib Solubility and Absorption in Gastric Acid-Suppressed Rat Model

Huda Jassim Muhammad[1], Tsutomu Shimada[2] and **Arimi Fujita[2]**

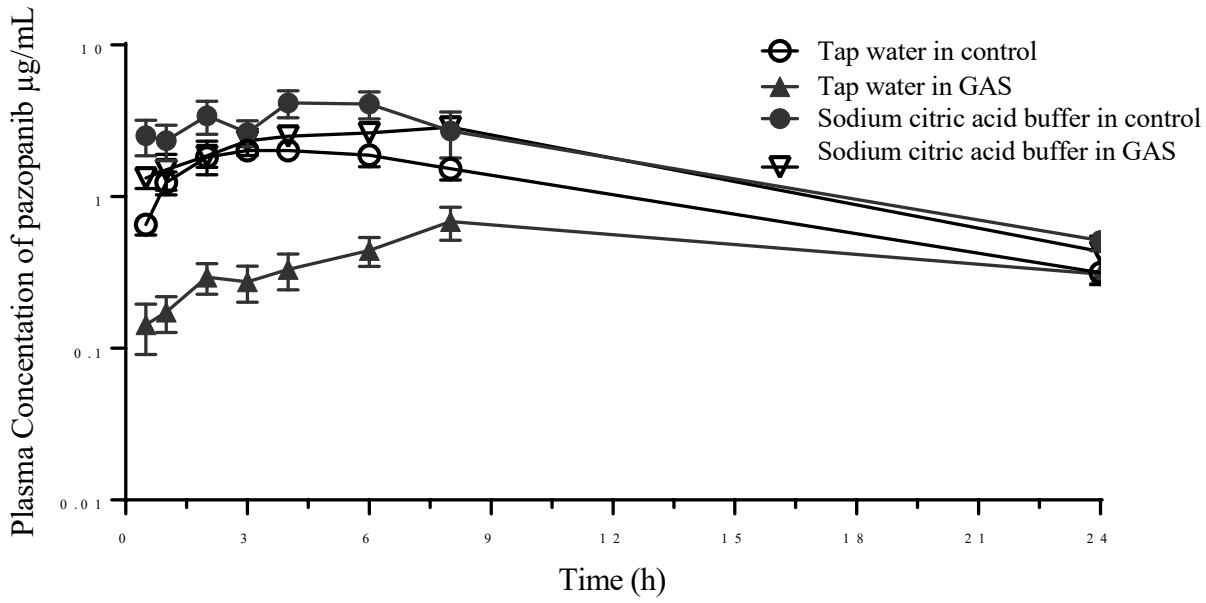
[1]Karbala University, Iraq
[2]Kanazawa University, Japan

The low solubility and variable absorption of pazopanib in gastric acid-suppressed conditions pose a significant challenge to its therapeutic efficacy. This study investigates the potential of a sodium citrate buffer system to improve pazopanib solubility and absorption in a gastric acid-suppressed rat model. The objectives of the study were to evaluate the solubility enhancement of pazopanib in the presence of sodium citrate buffer and its subsequent effect on absorption.

Methods included solubility studies conducted in different buffer solutions, followed by *in vivo* absorption tests in rats with induced gastric acid suppression. Preliminary studies were also carried out to determine the optimal dose of an acid-suppressing agent required to effectively inhibit gastric acid secretion in the animal model. The pharmacokinetic parameters of pazopanib, including plasma concentration and bioavailability, were analyzed after oral administration.

The results showed that pazopanib solubility significantly increased in sodium citrate buffer compared to standard conditions. *In vivo* absorption studies further demonstrated a marked improvement in the plasma concentration of pazopanib in gastric acid-suppressed rats when administered with sodium citrate buffer. The enhanced solubility and absorption were attributed to the buffering capacity of sodium citrate, which maintained an optimal pH environment for drug dissolution despite gastric acid suppression.

In conclusion, the sodium citrate buffer system effectively enhances pazopanib solubility and absorption under conditions of reduced gastric acidity. This approach holds promise for improving the oral bioavailability of pazopanib in patients on gastric acid-suppressing medications, providing a potential solution for overcoming drug absorption variability.



Plasma concentration-time profile after single oral administration of 7.5 mg/kg of pazopanib to control and esomeprazole rats with either tap water (pH 8.0) or citric acid buffer (pH 2.3). Values were represented as mean ± SE (n=6).

Pazopanib suspension in tap water (pH 8.0) and 0.1 M citric acid (pH 2.3) were shacked for 30 min, and orally administered to control and ESP rat after 2 hr of saline or esomeprazole administration (n=6).

Biography

Dr. Huda is a pharmacist and researcher with a strong background in clinical pharmacy. She completed her bachelor's degree in 2013 among the top 5 in her class, which led to her appointment as a pharmacist intern at her college. Dr. Huda then gained valuable experience working for five years (2014–2019) as a clinical pharmacist in both hospital and community settings. Driven by her passion for clinical pharmacy, she pursued further education and successfully enrolled in Iraq's competitive program to become a board-certified clinical pharmacist. During this time, she also applied for and was awarded the prestigious MEXT scholarship in 2020 to study abroad, fulfilling her dream of experiencing different academic approaches. She completed her graduate studies in clinical pharmacokinetics at Kanazawa University in Japan in 2022. After returning, Dr. Huda was promoted to the position of lecturer assistant at her college, where she continues to contribute to the field of clinical pharmacy through teaching and research.

Effect of *Melia azedarach* Seed Mediated Nano-ZnO on Growth Performance, Protein Utilisation Efficiency, Haematology and Nutritional Status in Pigs

Enathi Dinga, Upenyu Marume and **Getrude M Chelopo**

North West University, South Africa

The current study was conducted to investigate the effect of *Melia azedarach* seed-mediated ZnO nanoparticles on growth performance, protein utilisation efficiency, haematology and nutritional status in pigs. A total of 48 pigs were allocated to the following six treatments replicated 8 times: Negative Control (NC, No antibiotic), Treatment 2: Positive control (PC) given a conventional antibiotic (Oxytetracycline, 40 mg/kg feed); Treatment 3: Nano-ZnO 300 mg/L (N300ZnO), Treatment 4: Group given 150 mg/L *Melia azedarach* seed mediated nano-ZnO (N150MA), Treatment 5: Group given 300 mg/L *Melia azedarach* seed mediated nano-ZnO (N300MA), Treatment 6: Group given 450 mg/L *Melia azedarach* seed mediated nano-ZnO (N450MA). The experiment was conducted over 7 weeks. *Melia azedarach* seed-mediated ZnO nanoparticles had no significant effect on growth performance apart from average daily feed intake (ADFI) with treatment 3 having the highest value. It also improved growth performance and cumulative weight gain when compared to conventional antibiotics. The green synthesized nanoparticles significantly affected protein consumption and growth efficiency but not protein efficiency ratio and specific growth rate. *Melia azedarach* seed-mediated ZnO nanoparticles had no significant impact on nutritional parameters, serum minerals apart from phosphorus which can negatively affect renal functioning.

Biography

Ms. Enathi Dinga is currently working at the Agricultural Research Council, completed her Masters in Animal Sciences with a Cum laude at North West University, South Africa. Her research interests are focused on the use of nanotechnology in animal production, in particular, the exploration of nano-compounds in combination with phytochemicals as potential replacements for conventional antibiotics. She believes she could contribute significantly to the safe production of animal products for the benefit of consumers.

Social Determinants for the use of Complementary and Alternative Therapies among Women During Pregnancy, Labor and Postpartum Period in Low Income Countries: A Scoping Review

Mabel K. M. Magowe and **Norman Karl Swart**

University of Botswana, Botswana

Introduction and objective

Complementary and alternative therapies (CAM) use is reported worldwide, ranging between 36 to 62%. Africa and Asia are leading at 80%. CAM is used for socio-economic reasons, but it can have positive and adverse outcomes on the mother-baby dyad, requiring further research and interventions.

Scope

The purpose and scope of the project was to explore social determinants for the use of CAM among women during pregnancy, labor and the postpartum period, in low resourced countries, to suggest interventions that promote informed use and safety.

Methods used

A scoping review was conducted in Web of Science, Google Scholar, PubMed, and EBACOHOST. Key words used were: "Complementary AND alternative therapies AND Pregnancy AND Labor, AND post-partum AND low resourced settings". Full text, published between 2019 and 2024, relevant to the topic, were reviewed. The review and screening processes were presented in a PRISMA diagram. The accepted articles were presented in a table and were synthesised to guide discussion and conclusions.

Results

Social determinants of CAM use among the study population have been identified including positive experiences with symptom and side effects management, lack of knowledge about adverse effects, popular culture and low access to conventional medicines.

Discussion

Women use CAM for positive health outcomes because of socio-economic disadvantages, but demonstrate low knowledge of potential negative outcomes such teratogenicity for the fetus, requiring more education and research.

Conclusion

Further research and education to explore social determinants to address the benefits and threats of CAM use, especially teratogenicity and drug interactions.

Biography

Professor Mabel Magowe is an Associate Professor in the School of Nursing, Deputy Dean and Acting Dean in the Faculty of Health Sciences, University of Botswana. She has a PhD in Nursing, Master of Science with specialty in Midwifery, and a Bachelor of Nursing Education. Her research focus is on behavior change communication to prevent and control sexually transmitted infections, HIV, and unplanned pregnancies among adolescents and young women in Botswana, and understanding of social determinants that influence behavior and health outcomes. She has recently submitted a grant application on Intensifying Postpartum Follow-up Using USSD/IVR technology.

She has contributed immensely to teaching, clinical practice guidelines and students research skills through graduate and undergraduate supervision, served as an internal and external examiner at national and regional universities and ethical review committees at the University and Ministry of Health. Her research outputs include 38 peer reviewed publications, book chapters, and conference proceedings.

Advancing Vibrational Spectroscopy for Biomedical Applications

Maria Cristina Gamberini[1], Graziella Pellegrini[1] and **Hugh J. Byrne[2]**

[1]Department of Life Sciences, University of Modena and Reggio Emilia, Modena, Italy
[2]FOCAS Institute, Technological University Dublin, Ireland

The emergence of vibrational spectroscopy as a non-invasive biomedical tool is revolutionizing diagnostic screening, drug discovery, and personalized medicine. Vibrational spectroscopy provides a molecular fingerprint of biological samples, offering label-free, high-resolution insights into cellular and subcellular processes. The concept of Spectralomics expands this potential by analyzing entire spectral profiles rather than isolated biomarkers, similar to paradigms in genomics, proteomics, and metabolomics. This study explores Raman spectroscopy, which measure molecular bond vibrations, into biomedical applications. We propose a holistic approach leveraging a multivariate data analysis to extract disease-specific spectral signatures by utilizing confocal Raman micro spectroscopy, we analyzed the spectral responses of human cells under different conditions, detecting molecular-level changes in response to external stimuli. We would like to demonstrate that vibrational spectra can track cellular processes dynamically, providing insights into cellular metabolism, drug interactions, and disease progression. Furthermore, this approach aligns with the EU Directive 2010/63/EU, which promotes the reduction and replacement of animal testing through *in vitro* techniques. The integration of Spectralomics into biomedical research could enhance preclinical drug screening, improve toxicity assessment, and provide a deeper understanding of disease mechanisms at the single-cell level. These findings suggest that Spectralomics could become a cornerstone in next-generation biomedical diagnostics and drug development, shifting the paradigm from biomarker-based analysis to a more comprehensive, data-driven spectral interpretation.

Biography

Dr. Maria Cristina Gamberini is a professor at the University of Modena and Reggio Emilia, specializing in pharmaceutical chemistry, vibrational spectroscopy, and nanomaterials. She earned her degree in Chemistry and conducted research at the École Polytechnique Fédérale de Lausanne (EPFL, Switzerland) on nanomaterials and spectroscopic techniques.

Dr. Gamberini has published over 60 research articles in SCI(E)-indexed journals with an H-Index of 22. She collaborates internationally on projects in nanotechnology, crystallography, and pharmaceutical analysis. Her recent research focuses on the application of Raman and SERS spectroscopy for biomedical diagnostics and drug discovery.

She has been an invited speaker at international conferences and serves as a reviewer for major journals in analytical chemistry and nanotechnology.

Silver Nanoparticles as SERS Substrates for Enhanced Raman Spectroscopy in Antimicrobial Drug Analysis

Maria Cristina Gamberini

Department of Life Sciences, University of Modena and Reggio Emilia, Modena, Italy

Raman spectroscopy is a widely used vibrational technique in chemical and pharmaceutical analysis, providing molecular fingerprinting with minimal sample preparation. However, its application is often limited by fluorescence interference and low signal intensity, which reduce detection sensitivity. Surface-Enhanced Raman Spectroscopy (SERS) overcomes these limitations by exploiting localized surface plasmon resonance (LSPR) in noble metal nanostructures to enhance Raman signals by several orders of magnitude. This study presents the synthesis and characterization of silver nanoparticles (AgNPs) as SERS-active substrates for improving Raman analysis of antimicrobial compounds. A seed-mediated growth method was employed to obtain monodisperse AgNPs, ensuring better reproducibility and uniformity than the conventional Lee-Meisel synthesis. The nanoparticles were characterized using transmission electron microscopy (TEM) to evaluate their morphology and size distribution. To assess their effectiveness as SERS substrates, pure antimicrobial drugs were analyzed at concentrations ranging from 10^{-3} to 10^{-6} M. The results demonstrated a significant enhancement of Raman signals while reducing fluorescence interference. The increased signal intensity was attributed to the formation of "hot spots" in nanoparticle aggregates, where electromagnetic field amplification is maximized. These findings highlight the potential of AgNP-based SERS substrates as a non-destructive, highly sensitive analytical technique for detecting low-concentration pharmaceutical compounds. This study contributes to the advancement of nanotechnology in pharmaceutical spectroscopy, offering new opportunities for rapid and precise drug characterization. The optimized synthesis of monodisperse AgNPs provides a robust and scalable approach for high-performance SERS applications in the pharmaceutical field.

Biography

Dr. Maria Cristina Gamberini is a professor at the University of Modena and Reggio Emilia, specializing in pharmaceutical chemistry and nanomaterials. She earned her degree in Chemistry and conducted research at the École Polytechnique Fédérale de Lausanne (EPFL, Switzerland) on nanomaterials and spectroscopic techniques. Her work focuses on solid-state chemistry, Raman and SERS spectroscopy, and drug analysis.

Dr. Gamberini has published over 60 research articles in SCI(E)-indexed journals with an H-Index of 22. She collaborates internationally on projects related to nanotechnology, crystallography, and pharmaceutical analysis. Her recent research includes the synthesis of silver nanoparticles for enhanced Raman detection of antimicrobial drugs.

She has been an invited speaker at international conferences and serves as a reviewer for major journals in analytical chemistry and nanotechnology.

The Creative Process in Scientific Discovery

Albert Rothenberg

Harvard Medical School, USA

In an archived and unpublished but authenticated manuscript entry entitled, "The fundamental idea of general relativity in its original form", Albert Einstein wrote that, in 1907, during the course of working on a summary essay on special relativity for the Jahrbuch für Radioactivität und Elektronik he had generated what he called the "happiest thought of my life." This thought was the following:

"For an observer in free fall, e.g. from the roof of a house, there exists for him during his fall, no gravitational field." [italics original]

Applying what he has called his characteristic method of using "thought experiments," he went on to state that if the observer released any objects, they would remain "in a state of uniform motion and the observer was 'justified' in considering himself in a state of rest."

Next, he wrote the explanation of the physical basis of this thought which made the conclusion so gratifying: "The extraordinarily curious empirical law that all bodies in the same gravitational field fall with the same acceleration immediately took on, through this consideration, a deep physical meaning. For if there is even one thing which falls differently in a gravitational field than do the others, the observer will discern by means of it that he is falling in it. But if such a thing does not exist--as experience has confirmed with great precision--the observer lacks any objective ground to consider himself as falling in a gravitational field. Rather, he has the right to consider his state as that of rest, and his surroundings (with respect to gravitation) as field-free".

Two aspects of this account must be immediately striking: first, Einstein's passionate search and emotional involvement in his finding; second, the contradictory and oppositional nature of the elements in his conclusion, that is, a man falling from the roof of a house is both in motion and at rest at the same time. This conception is an aspect of the form of creative cognition I have termed the "janusian process." The term is based on the Roman god Janus, who was the god of beginnings and doorways and whose multiple faces (2,4,or 6, on the basis of the number of opposing doorways in the usual Roman stone dwelling) faced in diametrically opposite directions at the same time.

The janusian process consists of actively conceiving and using multiple opposites or antitheses simultaneously. The process usually occurs early in creative endeavors, and although out of the ordinary and sometimes sudden, it is conceived and used in a clear and logical frame of mind. It was a crucial aspect of Einstein's breakthrough to the General Theory of Relativity and there is evidence for its operation in other important scientific creative processes as well. Einstein elaborated his breakthrough into a theory reconciling Newton's laws of gravitation and his own special theory of relativity. He proposed the complete physical equivalence and simultaneity of the opposite effects of a uniform gravitational field in a non-accelerating or inertial frame and the effects of a uniformly accelerating or non-inertial reference frame. This led to his later theory of the universe curved as a geometric system of space-time.

Janusian Process

The janusian process, most commonly operative in the early or inspiration phase of creative production, consists of actively conceiving and using multiple opposites or antitheses simultaneously. The term, based on the multifaced (variously possessing two, four, or six faces) Roman god Janus looking always in diametrically opposed directions, denotes conscious conceptualization during the creative process of simultaneously coexisting and operative opposite or antithetical ideas, propositions, or actions. Although seemingly illogical and self-contradictory, creators construct these conceptualizations in rational states of mind in order to produce creative effects. In art and literature, they are responsible for early conceptions of plot, character, metaphor, organization, and design; in music for compositional construction; in science for creative breakthroughs, theorizing, and experiments. Depending on the level of development of a creative product, the janusian process also operates at later critical junctures and with practical solutions in a wide variety of fields.

Simultaneity of the multiple opposites or antitheses is a cardinal feature of the janusian process. Creators conceive firmly held propositions about the laws of nature, the functioning of individuals and groups, or the aesthetic properties of visual and sound patterns as simultaneously true and not true; harmonious and non-harmonious; or, both opposite and antithetical propositions are entertained as concurrently operative. A person running is both in motion and not in motion at the same time, a chemical is both boiling and freezing or kindness and sadism operate simultaneously. Previously held beliefs or laws are still considered valid but opposite or antithetical beliefs and laws are formulated as equally operative or valid as well.

These formulations within the janusian process are waystations to creative effects and outcomes. They interact and join with other cognitive and affective developments to produce new and valuable products. Creative homospatial and sep-con articulation I have described particularly operate as later unifying processes. Analogical, dialectic, inductive, and deductive reasoning are applied also in the development of theories, inventions, and artworks.

The janusian process initially disrupts preexisting contexts and conceptions. Highly surprising, even incredible, and inconceivable, are propositions that the contradiction or opposite of well-grounded fact, theory, or actuality is simultaneously valid. Previously held ideas and systems of ideas are split apart and broken, even essentially destroyed. This disruption engenders the development of something new.

In an extensive psychological interview study I have conducted with 36 Nobel laureates in the sciences, I have discovered the following creative manifestations of the janusian process.

Nobel Laureate	Opposite Factor	Opposite Factor	Janusian Conception
Joshua Lederberg	mold Neospora	non-Neospora	Bacterial conjugation
Nicholas Bloembergen	negative temperature	low temperature	solid state maser
Elias J. Corey	synthesis	disconnection	retrosynthetic chemistry
Pierre-Gilles de Gennes	hydrophilic	hydrophobic	Janus grains
Walter Gilbert	bacterial genome	human genome	evolution
Dudley Herschbach	minima	maxima	electron structure
Arthur Kornberg	enzyme action	enzyme substrate	DNA polymerase in DNA synthesis
Jean-Marie Lehn	1)inside	1)outside	"crypts"--supramolecular
	2)concave	2)convex	
Jean-Marie Lehn	pure mixture	instructed (impure) mixture	instructed mixture paradigm
Jean-Marie Lehn	hydrogen bond	complementary hydrogen bond	janus particle??
Edwin M. McMillan	too high energy	too low energy	synchrocyclotron (synchrotron)
Edward Purcell	spins	inverted spins	negative temperature-
Charles Townes	low energy state [matter]	high energy state [radiation]	temperature inversion for stimulated emission (Maser)
And I have found the following personal and detailed personal documentation of the janusian process operating in the following great scientific discoveries.			
Albert Einstein	motion	rest	general theory of relativity
Niels Bohr	wave	particle	complmentarity
Hideki Yukawa	field size	particle size	maser
Max Planck	small values	large values	R, the quantum constant
Charles Darwin	favorable characteristics	unfavorable characteristics	natural selection

[i]A. Einstein, quoted by permission of Otto Nathan and Helen Dukas, Einstein Archives, Pierpont Morgan Library. Translation: G. Holton.

Biography

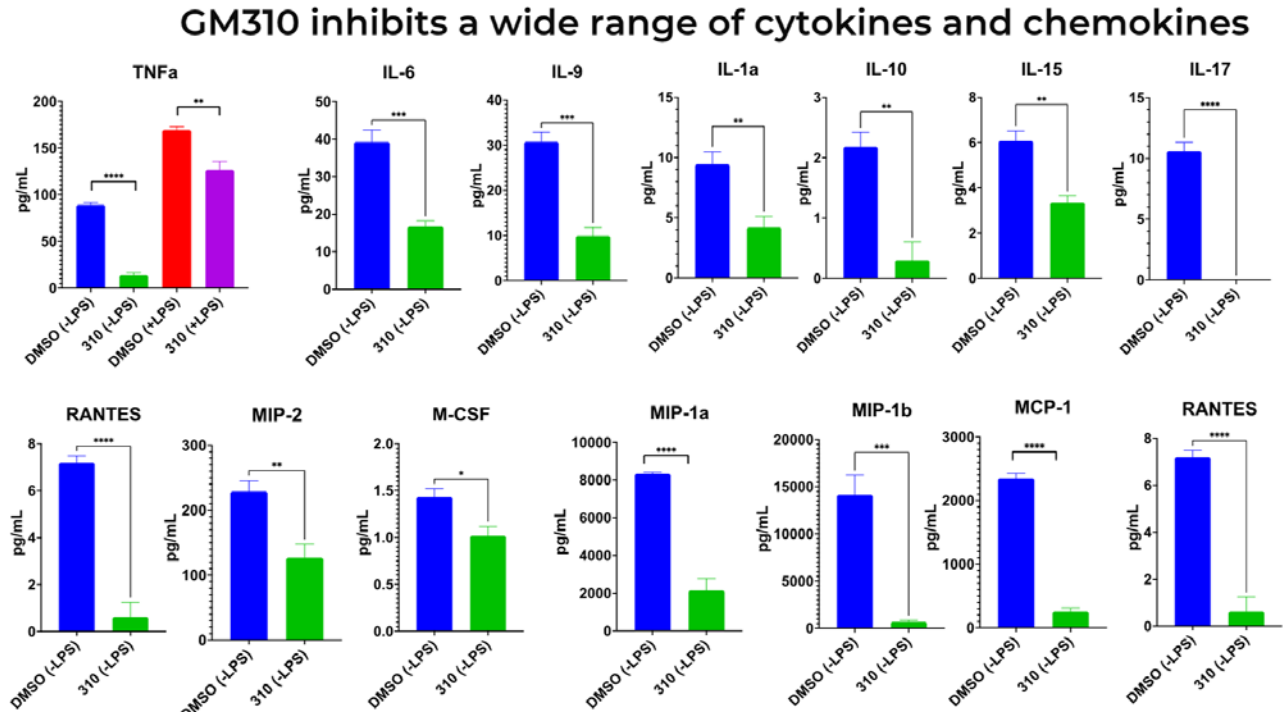
Albert Rothenberg is Professor of Psychiatry at Harvard Medical School, USA. He is the Principal Investigator of the research project “Studies in the Creative Process”, which focuses on the psychiatric and psychological bases of creativity in literature, art, psychotherapy, and science. His research focuses on creativity in science and art, world literature, and abnormal psychology. He has been a recipient of the Solomon R. Guggenheim Award, two NIMH Research Career Development Awards, Tufts Medical Alumni Award, Two Fellowships at the Center for Advanced Studies in the Behavioral Sciences, Fellowship at the Netherlands Institute for Advanced Study U.S. Army Certificate of Merit, the Golestan Award, and the Mesab Kovler Award. He is a twenty-five years long official nominator for the Nobel Prize in Physiology or Medicine.

Novel Small Molecules Mimic Molecular and Protective Effects of Dietary Restriction to Inhibit Proteotoxicity and Inflammation and Increase Lifespan

Charles Mobbs and **Rachel Litke**

Icahn School of Medicine at Mount Sinai, USA

To discover small molecules that would be effective to treat age-related diseases, we screened 2560 compounds (Microsource Spectrum library) for efficacy to delay Abeta proteotoxicity in C. elegans. The most protective compounds were, in order, phenylbutyrate, methicillin, and quetiapine, which belong to drug classes (HDAC inhibitors, beta lactam antibiotics, and tricyclic antipsychotics, respectably) which our studies had already indicated were promising to protect in neurodegenerative diseases. In addition to methicillin, several other beta lactam antibiotics also delayed Abeta proteotoxicity and reduced microglial TNF-a secretion, also implicated in age-related diseases. In addition to quetiapine, several other tricyclic antipsychotic drugs also delayed age-related Abeta proteotoxicity and increased microglial TNF-a, leading to the synthesis of a novel congener, GM310, which delays Abeta as well as Huntingtin proteotoxicity, inhibits LPS-induced mouse and human microglial and monocyte TNF-a, is highly concentrated in brain after oral delivery with no apparent toxicity, increases lifespan, and produces molecular responses highly similar to those produced by dietary restriction, including induction of Cbp, inhibition of inhibitors of Cbp, and genes promoting a shift away from glycolysis and toward metabolism of alternate (e.g., lipid) substrates, thus mimicking molecular effects of dietary restriction. GM310, as well as FDA-approved tricyclic congeners, prevented functional impairments and associated increase in TNF-a in a mouse model of stroke. Robust reduction of glycolysis by GM310 was functionally corroborated by flux analysis, and the glycolytic inhibitor 2-DG inhibited microglial TNF-a and other markers of inflammation, delayed Abeta proteotoxicity, and increased lifespan. These results support the value of phenotypic screens to discover drugs to treat age-related, especially neurological and even psychiatric diseases, including AD and stroke, and to clarify novel mechanisms driving neurodegeneration (e.g., increased microglial glycolysis drives neuroinflammation and subsequent neurotoxicity) suggesting novel treatments (selective inhibitors of microglial glycolysis).



Biography

Charles Mobbs obtained his bachelor's degree from MIT and PhD from USC, then carried out post-doctoral research at Rockefeller, where he was promoted to Assistant Professor. He then moved to Mt. Sinai School of Medicine where he is now a Professor in Neuroscience, Geriatrics, Endocrinology, and Pharmacology and Drug Discovery. His research has focused on the mechanisms mediating the general protective effects of dietary restriction to delay age-related diseases and increase lifespan. These studies led to the demonstration that a ketogenic diet can reverse diabetic kidney failure and neuropathy, as well as age-related kidney failure. For the last several years the Mobbs lab has increasingly focused on developing small molecules to mimic protective effects of dietary restriction and the ketogenic diet. One such small molecule is the focus of his presentation.

Discovery of Antibodies that Modulate Macrophage Functions in Boosting Cancer Immunotherapy

Jianyong Wang

Genentech, USA

As one of the most abundant cell types in many solid tumors, tumor-associated macrophages (TAMs) play critical roles in cancer progression. TAM is a type of immune cells characterized as high plasticity with both pro- and anti-tumor functions, depending on the environmental stimuli. On one hand, TAMs are capable of engulfing dying tumor cells, leading to the clearance of associated tumor antigens, which helps the tumor escape the host immune surveillance. TAMs also secret immune-suppressive cytokines that maintain a pro-tumor microenvironment. Consequently, TAMs contribute to the resistance of checkpoint inhibitors, chemotherapeutic agents, and adoptive T cell immunotherapies in clinic. On the other hand, when TAMs are properly activated, they can also actively engulf and destroy cancer cells and other pro-tumor immunosuppressive cells, acting as a defensive mechanism against tumors by killing them directly and indirectly. Thus, modulation of TAMs functions in tumors represents an attractive approach for cancer immunotherapy. Here, we share two case studies to exemplify that antibody drugs enhance cancer immunotherapy by modulating macrophage functions. First, we outline the discovery of anti-MerTK monoclonal antibodies (mAbs) that inhibit macrophage-mediated phagocytosis of apoptotic cancer cells both *in vitro* and *in vivo*. Dosing of anti-MerTK mAb in syngeneic mouse models resulted in robust anti-tumor responses when combined with anti-PD-L1, a checkpoint inhibitor that by itself only exhibited modest anti-tumor activity. Second, we will discuss how to exploit the antibody-dependent cellular phagocytosis (ADCP) function of TAMs to destroy regulatory T (Treg) cells, the major immunosuppressive cell type in tumors. More specifically, we discovered a specific mAb with enhanced antibody-dependent cellular cytotoxicity (ADCC) and ADCP that depletes the tumor-infiltrating Treg cells. In a syngeneic mouse tumor model, this specific mAb showed anti-tumor effects as a single agent and enhanced anti-tumor activities when combined anti-PD-L1.

Biography

Dr. Jianyong Wang is a senior principal scientist at Genentech with more than fifteen years of working experience in antibody drug discovery and development. His responsibilities include developing and implementing discovery strategies for antibody-based biologic drugs, driving and evolving antibody molecules from the earliest screening efforts to the characterization of the final clinical candidate. He is also interested in adapting and evolving innovative technology platforms to facilitate discovery of the next generation of biologic drugs. Dr. Wang has a research interest in the roles of macrophages in various health conditions. Macrophages are versatile immune cells that can modulate inflammation, tissue repair, and tumor progression. Dr. Wang's recent research aims to understand macrophage functions in different pathological conditions, in order to develop novel drugs that modulate their activities in diseases and improve clinical outcomes.

Guiding the Repair Process

Prof. Dr. Marcos Barbosa Salles[1], Prof. Dr. Marcelo Yoshimoto[1], Prof. Dr. Elio Hitoshi Shinohara[2] and **Prof. Dr. Sergio Allegrini Jr[3]**

[1]Marcelo Yoshimoto Institute, Brazil
[2]Depart. Oral and Maxillofac. Surg. Hospital Regional de Osasco SUS/São Paulo Brazil
[3]Católica Portuguesa University (UCP), Viseu Portugal

How far can we go to repair lost or atrophic tissues? This is a question that countless researchers ask themselves and strive to answer. The use and improvement of surgical techniques and the advancement of tissue and cellular engineering are important tools to develop new therapies and expand knowledge of the multiple facets involved in promoting the repair of damaged tissues and organs. Our work is based on biomimetics, a relatively recent new concept that aims to understand and efficiently reproduce biological logic, resulting in two distinct materials: mimetic-oss and mimetic-nv, the first for stimulating bone neoformation and the second for repairing peripheral nerves. With topical application, we use vitamin components and mineral salts associated with a collagen matrix that, in addition to being biocompatible and fully absorbed promote an environment favorable to the neoformation of the target tissue. This has been observed in both laboratory animals and humans [1-6]. Previous studies have histologically observed a model of ossification called transchondroid, a transdifferentiation of fibroblasts into cells that produce bone matrix, in addition to a significant increase in bone matrix proteins, such as osteocalcin and osteonectin, resulting in a higher rate of local bone deposition. In the peripheral nervous tissue, after neuropraxia of the sciatic nerve of Wistar rats, the formation of a bridge of nervous tissue between the distal and proximal stumps was observed, justifying the subsequent results in mandible fractures observed in humans, which resulted in a significant reduction in the time of paresthesia in patients treated with this formulation [1;2;5]. However, there was still some doubt regarding the involvement of the material in the intracellular environment, which was resolved with another study in which we evaluated the activity of the transcription factor NF-kB in osteocytes of Wistar rats after surgical trauma. The results indicated a statistically significant reduction in the activation of this transcription factor in animals treated with mimetic-

oss [3;4;6]. Despite the unorthodox approach of these studies, the results in laboratory animals and humans have often demonstrated surprising results, indicating their viability as a therapeutic tool for functional recovery and improvement of patient's quality of life. Regarding the initial question “How far can we go to repair lost or atrophic tissues?” I don’t know the answer, but I like to think that we have taken a small step toward achieving our goal.

Biography

Graduated in Dentistry from Universidade Paulista (UNESP), post-graduated Master's and PhD from Universidade de São Paulo (USP), post-doctorate in materials from PUC/RS, Specialist in Implants. His area of interest is related to research and development of biomaterials, with two patents already registered. He also has experience in the development of clinical research. Currently not linked to an educational or research institution, He works in a private practice.

Human Plasma Kallikrein/ Kinin and Plasminogen Activation Systems: A Crosstalk in Breast Cancer

Guacyara Motta

Departamento de Bioquímica, Escola Paulista de Medicina, Universidade Federal de São Paulo, Brazil

Human plasma prekallikrein (PK) and high-kininogen (HK) are proteins from contact system discovered as actors in coagulation, fibrinolysis and inflammation. Urokinase plasminogen activator (uPA) and the receptor (uPAR) contribute to aggressive phenotype in breast cancer and form a complex on cell surface. The PK active form (PKa) activates pro-uPA interconnecting plasma kallikrein-kinin (KKS) and plasminogen activator (PAS) systems. Syndecans (syn) are proteoglycans that mediate binding and endocytosis of protein complexes. Our objective is to characterize the interaction of proteins from KKS and PAS in breast cancer cells. HK binding to cell surface and bradykinin (BK) release in supernatant, determined by radioimmunoassay, were found in MDAMB-231 (highly-metastatic) > MCF-7 (less-metastatic). The kininogenase activity was mediated by serine-protease and the results support the proliferative effect of BK. Using confocal microscopy we found in MDA-MB-231, uPAR colocalized inside with syn-1 (70%) and syn-4 (94%); uPA-syn-1 colocalization was low but uPA-syn-4 colocalized better inside (67%); PKa-uPA colocalization was 60% either on surface or inside. In MCF-7 more uPAR was found on surface and uPA inside. Syn interaction with uPAR and uPA may mediate uPAR-uPA endocytosis. PKa was detected on surface and into lysosomes in both cell lines and in MCF-7, PK mRNA expression was 10 times lower compared to MDA-MB-231. The migration was little reduced in presence of 4-Cl (uPA-inhibitor) and PKSI (PKa-inhibitor), respectively in MCF-7 and MDA-MB-231. The enzyme assays with chromogenic substrates showed in MDA-MB-231 uPA activity reduced to 80% and 74% respectively in presence of PKSI and 4-Cl, but PKa activity was not influenced. In MCF-7 lysate immunodetection showed uPA, PKa light-chain (active site) and none uPAR; MDA-MB-231 lysate showed uPA, uPAR but none PKa. Our data support a crosstalk between KKS and SAP in breast cancer where PKa may play role in scuPA activation and suPAR release after uPAR cleavage.

Biography

Guacyara Motta's graduation was in Biological Sciences at Escola Paulista de Medicina, Universidade Federal de São Paulo (EPM/UNIFESP); her Master degree was in Molecular Biology at EPM/UNIFESP and her PhD was in Molecular Biology at EPM/UNIFESP. During her PhD program she was trainee at the Division of Clinical Chemistry and Biochemistry, University of Munich (Ludwig-Maximilians), Germany and her postdoctoral training was at the Department of Internal Medicine, Division of Hematology/Oncology, at the University of Michigan (Ann Arbor), USA. Currently she is an Associate Professor in the Department of Biochemistry at EPM-UNIFESP. Her expertise is in the area of Biochemistry, with emphasis on Protein Chemistry, Intermediate Metabolism and Cellular Biology. Her research topics are mainly focused on plasma kallikrein-kinin system proteins, plasma (pro) kallikrein (PK/PKa) and kininogens (HK/LK), and fibrinolysis proteins, urokinase (uPA) and its receptor (uPAR), regarding the structure, function and interaction of these proteins with cell biology.

Comparing the Generalizability of Reliability-Based vs. Accuracy-Based Diagnostic Models in Medical and Healthcare Applications

Sepideh Etemadi[1] and **Mehdi Khashei**[2]

[1]Department of Mechanical and Industrial Engineering, University of Minnesota Duluth, USA
[2]Department of Industrial and Systems Engineering, Isfahan University of Technology, Iran

Various approaches with different structures and characteristics have been proposed as tools to address diverse health and medical prognostic and diagnostic issues. Despite the differences among these modeling methods, they all focus on maximizing the accuracy or reliability of the outcomes to obtain the most generalizable model. Although reliability theoretically plays a crucial role in enhancing generalization capability, especially in high-risk decisions, many models for tasks such as causal prediction, time-series forecasting, and classification have primarily been developed with a focus on maximizing accuracy. Hence, the primary objective of this study is to emphasize the relative importance of accuracy- and reliability-based methodologies on the quality of medical decisions made in intelligent and statistical decision support systems, as well as to determine their impact. To achieve this, 33 diverse datasets from the UCI database, spanning causal, classification, and time series categories, have been analyzed. These datasets cover various scopes, including cancer and disease diagnosis, experimental therapy, and fertility prediction. Empirical results indicate that the reliability-based methodology achieved improvements over the accuracy-based approach: 2.26% in causal prediction cases, 13.49% in classification cases, and 3.08% in time-series forecasting cases. Overall, the reliability-based approach resulted in a 6.28% improvement compared to similar accuracy-based models. As a result, the findings of this study indicate that reliability is a more effective factor than accuracy in improving the quality of decisions made by models in medical-related issues. Ensuring the reliability of model performance is essential for achieving stable and appropriate predictions in medical areas such as disease prediction, medical diagnosis, and clinical data modeling, thereby facilitating decision-making. Consequently, reliability-based models with the capability to model uncertainty are more suitable for addressing real-world medical decision-making problems.

Biography

Sepideh Etemadi received her M.Sc. and Ph.D. degrees in Industrial Engineering from Ferdowsi University of Mashhad and Isfahan University of Technology (IUT) in 2014 and 2022, respectively. She is currently a postdoctoral associate at the Department of Mechanical and Industrial Engineering, University of Minnesota Duluth, USA. Her main research interests include modeling and forecasting, data mining, machine learning, and optimization.

Mehdi Khashei received his M.Sc. and Ph.D. degrees in Systems Engineering and Industrial Engineering from the Isfahan University of Technology in 2005 and 2013, respectively. He is currently an assistant professor at the Department of Industrial and Systems Engineering, Isfahan University of Technology (IUT), Iran. He is the author or co-author of several scientific papers in international journals or communications to conferences with reviewing committees. His main research interests include Artificial Intelligence; Soft Computing; Time Series Forecasting; Classification and Clustering, Soft Intelligent decision-making; and Financial Management and Engineering.

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