

Proceedings of
International E-Conference on

PHARMACOLOGY & TOXICOLOGY

December 01-02, 2020 | Webinar



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DAY 1 | **KEYNOTE SPEAKERS**

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**Amal Saad-Hussein**Environmental & Occupational Medicine Department, National Research Centre,
Cairo, Egypt

Role of Molecular Epidemiology in Prediction of Cancer Among Tobacco Smokers

Tobacco smoke is common unacceptable habit worldwide, and among the various histologic types of lung cancer, cigarette smoking had the strongest effects on small cell carcinoma, followed by squamous cell carcinoma and adenocarcinoma. Gene susceptibility to cancers among smokers was discussed and proved in several studies. Therefore, it is important to define the predictive role of molecular epidemiology in prediction of cancers among tobacco smokers. This presentation will summarize the recent trends of using epigenetics, gene polymorphism, comets assay, telomere length, and other biomarkers in prediction of cancers in smokers compared to nonsmokers. These molecular biomarkers proved to have significant effects in early prediction of cancers among smokers

Keywords: Smoking, Cancer, Epigenetics, Gene polymorphism, Comets Assay, Telomere length

Biography:

Amal SaadEldin Ahmed Hussein is an Emeritus Professor of Environmental Health & Preventive Medicine, Environmental & Occupational Medicine Department, National Research Centre, Egypt Former Dean of Environmental Research Division, and Former Head of Environmental & Occupational Medicine Department, NRC, member in National Committee of Toxicology, Academy of Scientific Research and Technology, and expert in IPCC, and reviewer several international journals. Ph.D., M.D., MPH were in Public Health and Environmental Medicine from Faculty of Medicine, Cairo University, and obtained several scientific prizes, and Certificates of Excellence in Scientific Productions. She is General Sectary for PAEMGS, and Deputy Head of EEMS. She established Smoking Cessation clinic and Environmental Toxicology Clinic in NRC. She has 72 International and 21 National Publications, and she was the principle investigator of several national projects.

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**Alejandro Sánchez-Melgar*, José Luis Albasanz, Mairena Martín**University of Castilla-La Mancha, Department of Inorganic, Organic and Biochemistry.
Ciudad Real, Spain

Resveratrol acts as Adenosine Receptors Agonist: Potential Benefits for Human Health

Resveratrol (RSV) is a natural polyphenolic compound occurring in plants such as peanuts, berries and red wine, among others. This phytochemical has shown multiple beneficial properties for human health, but the precise mode of action remain to be clarified. Therefore, the aim of this work was to investigate whether RSV was able to modulate adenosine-mediated signaling *in vitro* (rat C6 glioma cells) and *in vivo* (brain from SAMP8 mice). Our biochemical and computational analysis in C6 cells showed that RSV directly binds to adenosine receptors and acts as a non-selective agonist on these receptors. RSV-induced receptor activation can stimulate or inhibit adenylyl cyclase (AC) activity in a concentration-dependent manner. RSV also modulated gene expression and receptor levels of adenosine receptors, and their downstream AC pathway. Furthermore, RSV induced cell growth inhibition on C6 cells in a time- and concentration-dependent manner, cell cycle arrest and caspase-3 activation. Furthermore, pharmacological inhibition of A2A receptor partially mimicked the effects caused by RSV. On the other hand, long-term diet supplementation with RSV induced changes on gene expression as well as transduction pathways mediated by adenosine receptors in brain from SAMP8 mice. RSV increased levels of A1 receptor, whereas no changes on A2A receptors were detected. Concerning their functionality, A1 receptor was found to be potentiated, however, A2A receptor was desensitized after RSV supplementation. In addition, 5'-Nucleotidase and Adenosine Deaminase were reduced by RSV, suggesting an alteration on adenosine metabolism. In conclusion, our results indicate that RSV modulates adenosine-mediated signaling in both *in vitro* and *in vivo* models. Therefore, new therapeutic strategies involving resveratrol and adenosine receptors should be aimed in the future for a variety of diseases such as cancer and neurodegenerative diseases.

Keywords: Resveratrol, Adenosine Receptors, GPCR, Neurodegeneration, Cancer.

Biography:

Alejandro Sánchez Melgar is a Assistant professor of Biochemistry/Department of Inorganic, organic and biochemistry/University of Castilla-La Mancha. He graduated in Biology and recently received my doctoral degree by the University of Castilla-La Mancha in 2017. I am author of 6 research paper since 2017. My research interest lies on how natural polyphenols such as resveratrol can benefit human health, particularly cancer and neurodegenerative diseases. In this line, my work is mainly focused on how adenosine-mediated signaling, a key regulator of the neurotransmission, is affected in the neurodegeneration process, with special emphasis on how resveratrol modulates adenosinergic system.



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Exploring the Bioactivities of *Boswellia serratta* Extract through *in Vitro*, and *in Silico* Studies

Dr. M. Maghimaa^{2*} and Ramsi V¹²Muthayammal College of Arts and Science, Rasipuram, Namakkal DT. Tamilnadu, India.¹Principal Investigator, S & T Project, TNSCST (DST-Grant)

Hospital-acquired nosocomial infections represent the most important public health crisis at a global level. They are a consequence of key causes of mortality and morbidity, and economic hardship among the hospitalized cases. Soft tissue, surgical wound, respiratory tract, bloodstream, and urinary tract infections are the types of hospital-acquired Nosocomial infections. *Klebsiella oxytoca* was isolated from the wound sample and identified by microscopic observation and biochemical characterization. Antibacterial assay on the isolate was executed using the Kirby Bauer disk diffusion method. *Boswellia serratta* is one of the most often used ethnomedicinal plants by the ancient people of Tamilnadu. The present research was intended to investigate the antibacterial property of the ethanol extract of *B. serratta*. GC-MS study was employed to identify the bioactive compounds from *B. serratta* extract. Among the identified compounds, Alpha-Asarone (Dock score -5.5 kcal/mol), Carbonic acid (Dock score -4.5 kcal/mol), Cholan-24-oic acid 3,12-bis acetyloxy (Dock score -7.6 kcal/mol) were observed to exhibit better binding affinities with beta-lactamase proteins from *K. oxytoca* through molecular docking studies. In conclusion, this research finding scientifically sustained the ethnomedicinal exploit and worth of this plant, which may supply an impending resource for the future development of therapeutics. The ethanolic plant extract was observed to be vigorous against the pathogenic gram-negative bacteria such as *Klebsiella oxytoca*, representing its potential appliance related to nosocomial infections.

Keywords: Nosocomial Infection, Gram-Negative Bacteria, GCMS, Molecular Docking

Biography:

Dr. M. Maghimaa, Principal Investigator (S& T project, TNSCST), Assistant Professor, Department of Microbiology, Muthayammal College of Arts and Science, Rasipuram, Namakkal District, Tamilnadu, India.

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Natural Hypoglycemic Nanoparticles to Deliver Drugs to Diabetic Patients

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Nanoparticle-facilitated drug delivery is a promising tool in medicine nowadays with many important drugs being co-administered in this fashion along with nanoparticles made of polymer like PEG or other material. The prime concern is the safety and biocompatibility of nanoparticles used for the purpose. In this study, we have performed HF/6-31G calculations coupled with intermolecular interaction calculations and nanoscale molecular dynamics simulations to investigate self-assembly in curcumin induced by trigonelline. Similar to recently reported self-assembly in curcumin induced by sugar, trigonelline, a natural antidiabetic derived from fenugreek, can also induce auto-catalyzed self-assembly in curcumin to form nanoparticles. It has been shown that these nanoparticles may be utilized for the delivery of drugs with severe side effects especially for diabetic patients with triple benefit of being antidiabetic, biocompatible and safe. As an example, carriage of antidiabetic drug pioglitazone and anticancer drug taxol have been depicted utilizing nanoparticles of curcumin and trigonelline. Twenty five taxol molecules could be comfortably carried in a 50 nm nanoparticle with an average overall root mean square deviation of 2.89 Å with reference to initial positions. For the first time, this study shows the possibility of developing antidiabetic nanoparticles with plethora of opportunities for diabetic patients. The study is expected to motivate experimental verification and has a long lasting impact in medicinal chemistry

Keywords: Self-Assembly, Curcumin, Trigonelline, Nanoparticle, Drug-Delivery, MD Simulations

Biography:

Dr. Arpita Yadav is an Associate Professor, Department of Chemistry, University Institute of Engineering and Technology, Chhatrapati Shahu Ji Maharaj University, Kanpur, India

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Olive Oil and Figs as Efficient Natural Treatment During COVID-19 for Different Inflammatory Diseases

Tamer A. Addissouky

PhD, MLS ASCP, MLS MOH, MLS ASCP, USA, PhD biochemistry, Menoufia University, Egypt

Herbal medicinal products (HMP) and Traditional HMP contain herbal drugs (HD) or herbal preparations (HP) as effective pharmaceutical agents. The quality of HMP has approved its vital role in treating rather than other products. Natural compounds have been playing pivotal roles in motivating human health because of their several bioactivities, such as potent antioxidant and anti-inflammatory characters that could eliminate the risk of diabetes, cardiovascular, and cancer diseases. A randomized controlled clinical trial was designed. A mixture of Olive oil with figs fruit is a main important food component in Mediterranean dishes, which are linked to inferior risk of cardiovascular, diabetes, hypertension, and cancer diseases in addition to antiviral effect. 70 patients who had been infected with covid-19 and other chronic diseases depended on a mixture of olive oil with figs as a main dish for 7 days in comparison to coronavirus patients had never been given the same mixture during their disease's meantime. After a determined period, covid-19 cases who relied on a mixture as a main diet, repeated their investigation parameters and improvement had been noted in contrast with other cases. This plan study has been repeated many times and has approved the efficient role of olive oil with figs. In conclusion, in order to have effective results of treatment viral diseases, a mixture of olives oil with figs fruits should be recommended as a main diet during treating the patients who are infected with covid-19 and other chronic diseases. Most importantly, a mixture of olives oil with figs can be used as a protective agent against Geriatrics diseases such as diabetic, heart diseases and rheumatoid disease.

Keywords: Pharmaceutical Agents, Herbal Medicinal Products, Covid-19, Human Health, Investigation Parameters

Biography:

Dr. Tamer Abdelmoaty Addissouky Ali, MLS MOH, MLS ASCP, PhD Biochemistry, Menoufia University. Medical lab scientist and management member at ministry of health, researcher, editor and reviewer at many international journals, lecturer of biomedical sciences at nursing institute, author for many published articles

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Nano Medicine: A New Way to Treat Diabetes Mellitus

Dr. Shanker Kalakotla

Yonsei University, South Korea

Diabetes is a chronic metabolic disorder that affects millions of people worldwide and takes a heavy toll on human life. Traditional plant treatments have been used throughout the world for the therapy of diabetes mellitus. Among several medications and other alternative medicines, herbal drugs have been known to cure and control diabetes; additionally, they have no side effects. Newer drugs with the least side effects but with highest efficiency are being relentlessly searched by the researchers. Herbal drugs are very common in use in our day-to-day life easily available and are having least side effects. Nanotechnology is a branch of science and technology conducted at the nanoscale, which is about 1 to 100 nanometers. Nanoscience and nanotechnology are having a wide range of applications in fields, such as green chemistry, herbal drug research. With respect to herbal medicine the drug will take more time to show the anti-diabetic activity because herbal drugs are basically more insoluble in nature. To overcome this kind of problems nano herbal medicine is needed. Nano Medicine (NM's) are having less particle size, more surface area, more solubility which results in the optimum dose of drug that can reach to systemic circulation and onsite of action is very quick. Recent studies on the use of herbal plant extracts in synthesis of NM's are a relatively new and exciting area of research with considerable potential for development of new methods in nano medicine. NM's capable to treat diabetes effectively by having very less particle size comparatively with herbal medicine current review is an attempt to list of out the anti-diabetic plants, biosynthesis and various characterization methods of NM's and their advanced pharmacological applications to treat diabetes.

Keywords: Herbal Drugs, Nano Medicine (NM's), Diabetes Mellitus, Optimum Dose, Nanoscience and Nanotechnology

Biography:

Dr. Shanker Kalakotla completed schooling from Government High School, Ursu-Warangal and intermediate from CKM college Warangal. He has completed Diploma in Pharmacy from State Board of Technical Education & Training (SBTET), Bachelor of Pharmacy from Kakatiya University, Master of Pharmacy from Jawaharlal Nehru Technological University Hyderabad (JNTUH) and PhD from JNT University Hyderabad (JNTUH), India. He completed his Full-Time PhD, at the age of 29, under the supervision of Dr G Krishna Mohan, Professor of Pharmacy, Centre for Pharmaceutical Sciences JNTUH. He was the first alumni student to finish M. Pharm and full-time PhD from Centre for Pharmaceutical Sciences, IST, JNTUH University. He was a Senior Research Fellowship (SRF) awardee from Science & Engineering Research Board (SERB-DST), Professional PG scholarship awardee from University Grants Commission- New Delhi and two times travel grant receiver from CSIR and CICS respectively. He was first PhD candidate to receive Swaeroes Fellowship. He presented his PhD work in various international platforms like Singapore, Malaysia, Thailand etc., He has a given oral presentation on New Drug Development for the treatment of Diabetes, Liver Toxicity and Cancer using Nano Medicine in various conferences, seminars and workshops in India. He has published more than 29 research articles in international peer reviewed, science citation indexed reputed journals with more than 100 citations. He achieved 59 cumulative impact-factor of his total research articles published so far. He applied for 2 patents so far and waiting for the results. He gained Industrial R&D experience in one of top Healthcare company called GlaxoSmithKline GSK-Healthcare as a Scientist-R&D Innovation, Genome Valley R&D division Hyderabad, India. He is an editorial member and scientific reviewer for more than 8 international journals. Currently he is working as a Senior Post-Doctoral Research Fellow in School of Life Sciences, New Drug Development laboratory, Yonsei University, Seoul, South Korea.



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DAY 1 | **POSTER PRESENTATIONS**

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Sorting of Exclusive Mitochondrial Enzymes from Databases: at the First Step of Studying Mitochondrial Enzymes as the Biomarker of Acute Aluminium Phosphide Poisoning

Deepak Yadav*, Rajasri Bhattacharyya and Dibyajyoti Banerjee

Department of Experimental Medicine and Biotechnology

Use of aluminium phosphide (ALP) for storage of food is a common practice in the developing world. The menace of acute ALP poisoning is also ongoing. ALP liberates phosphine gas which is a mitochondrial poison. Expectedly that is going to disrupt mitochondrial membrane and leak the mitochondrial proteins in the extracellular space. In other words, the mitochondrial proteins should be screened for biomarkers of acute ALP overdose. To take a systemic approach, we should get a total list of mitochondrial proteins. With this background, we have searched the dedicated mitochondrial database (Mitoproteome) and observed that some proteins are mentioned there are also available at other places. We will demonstrate our observation as we believe that the results of this investigation will help to understand which proteins are exclusively mitochondrial and which proteins are not. Needless to emphasize that this can be used for screening mitochondrial proteins/enzymes as biomarkers of ALP and other mitochondrial poison exposure.

Keywords: Poisoning, Biomarkers, Mitoproteome, Aluminium Phosphide, Mitochondrial Poison.

Biography:

Deepak Yadav is a Ph.D Student. Mitoproteome database, Uniprot, OMIM, NCBI Blast, The human protein atlas

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Neuroprotection by Brain-Derived Neurotrophic Factor in Experimentally Induced Huntington Disease

Ola E. Mohamed^{1*}, Ahmed M. Fayez¹, Dalaal M. Abdallah², Hanan El-Abhar³¹Pharmacology and Toxicology Department, Faculty of Pharmacy, MSA University²Pharmacology and Toxicology Department, Faculty of Pharmacy, Cairo University³Pharmacology, Toxicology and Biochemistry Department, Faculty of Pharmacy, Future University in Egypt

Huntington Disease (HD) is associated with aberrant multiple targets signaling to hasten neuronal death. In the present study, morin (MH) neuroprotective potential was tested in a model of 3-nitropropionic acid (3-NP)-induced HD. Rats were divided into 3 groups, the 1st served as a normal group, the 2nd received 3-NP for two weeks to induce HD, whereas the 3rd one was injected with both 3-NP and MO. MO was able to reduce motor deficits and enhance the AKT, brain-derived neurotrophic factor (BDNF) cue to boost neuroprotection. Meanwhile, it suppressed the cortical contents of nuclear factor- κ B, interleukin-1 β , tumor necrosis factor- α , and malondialdehyde. It is concluded that MO could hamper HD via enhancing BDNF, as well as its antioxidant and anti-inflammatory effects.

Keywords: Brain, BDNF, Morin, HD

Biography:

Ola Essam Mohamed is a Teaching Assistant at Pharmacology and Toxicology Department, Faculty of Pharmacy, MSA University

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4-Week Repeated Dose Rat GLP Toxicity Study of Oncolytic ECHO-7 virus Rigvir Administered Intramuscularly with a 4-week Recovery Period

Pēteris Alberts^{2,3*}, Katarzyna Piwoni¹, Gilta Jaeckel¹ and Agnija Rasa²¹Charles River Laboratories, East Lothian, UK.²Rigvir, Riga, Latvia,³Presenting author

The oncolytic ECHO-7 virus Rigvir was registered in Latvia in 2004 and later in Georgia, Armenia and Uzbekistan. No severe adverse events have been observed. The aim of this 4-week repeated dose good laboratory practice (GLP) toxicity study was to determine the potential toxicity and reversibility of any findings after a 4-week treatment-free period to meet regulatory requirements. Han Wistar rats were randomly assigned to control and Rigvir (2×10^6 , 1×10^7 and 2×10^7 TCID₅₀) groups. Intramuscular administration was on days 1-3, 8-10, 15-17, 22-24. Clinical signs, average food intake, body weights, ophthalmology, clinical pathology parameters, bioanalysis, gross necropsy, organ weights, biodistribution and histopathology were evaluated. There were no unscheduled deaths, adverse clinical signs, no changes in body weight, body weight gain, food intake, ophthalmoscopy, clinical pathology, urine volume or composition, or organ weights. Slightly higher numbers of eosinophils in Rigvir-treated animals returned to normal after recovery. Rigvir was biodistributed to the spleen. Low incidence of inflammatory cell infiltration at administration sites and increased lymphoid cellularity at the regional (inguinal and popliteal) lymph nodes were observed; after recovery, only those in popliteal lymph nodes remained. Therefore, it is concluded that the 4-week Rigvir (2×10^7 TCID₅₀) administration was well tolerated in rats. The no observed adverse effect level (NOAEL) was the highest dose tested, 2×10^7 TCID₅₀.

Keywords: ECHO-7 Virus, Oncolytic Virus, Rigvir, Virotherapy, Preclinical

Biography:

Pēteris Alberts, Head R&D, PhD, Pharmacologist Latvia.



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Martins-Ferreira, J

Cunha-Filho, G.A.; Noël F.; Santos, M.F. and Quintas, L.E.M.

What does Bufalin tell us about Changing Shape?

Cardiotonic steroids (CS) are now known to bind to $\text{Na}^+/\text{K}^+ - \text{ATPase}$ located in caveolae and transduce the extracellular signal to intracellular compartments via activation of different protein kinases, including Src tyrosine kinase-Ras-ERK1/2 pathway. Consequently, they regulate cell cycle and gene expression, thus playing an important role in the control of renal and cardiac functions. Fibrosis is characteristic of the advanced stages of chronic renal and cardiac disease. Epithelial to Mesenchymal Transition (EMT) is a biological process involved in the establishment of fibrosis. One of the first signs of EMT is the endocytosis of membrane E-cadherin and impairment of cell-cell adhesion followed by gene activation of SNAIL which in turn inhibits E-cadherin and enhances mesenchymal proteins, as vimentin gene transcription, resulting in a phenotype transformation. Src kinase has been shown to contribute to EMT in cancer. Recent studies have identified both ouabain and marinobufagenin as endogenous steroids whose production and secretion are regulated by multiple physiological and pathological stimuli including angiotensin II and epinephrine in human. This study aims to characterize the mechanism involved in CS causing EMT. For this purpose, LLC- PK1 epithelial cell cultures were exposed to bufalin, a CS purified from toad venom, and EMT characteristics along with Src-Ras-ERK1/2 signaling pathway were evaluated. EMT characterization and signaling pathway were evaluated by phase contrast and fluorescent microscopy, high content screening microscopy, surface protein biotinylation and immunoblotting assays at 4 or 24 hours after incubation with 20 nM bufalin. Results: Bufalin 20 nM treatment for 4 or 24 hours increased endocytosis of E-cadherin as shown by immunofluorescence staining and a decrease of almost 45% of surface/total E-cadherin ratio in 20 nM bufalin- treated cells ($n=3$, $p<0.05$) evidenced by surface biotinylation. In 24hours we detected a change from epithelial to fibroblast-like morphology in bufalin-treated cells, and those cells expressed a considerably higher content of stress fibers, whose formation was prevented by inhibition of Src (2 μM PP2) and MAP kinases (10 μM U0126) activation as well as changes in cell morphology. ERK1/2 activation increases around 120% in cells treated for 24 hours. Discussion: The $\text{Na}^+/\text{K}^+ - \text{ATPase}$ bufadienolide ligand bufalin activates Src and MAP kinase signaling pathway and causes EMT in cultured renal cells. Loss of surface E- cadherin expression is in between the first steps of EMT phenomenon and is induced by bufalin. These results indicate that CS may be a key player in cell differentiation and fibrosis common in later stages of kidney chronic disease. Defining the intracellular pathways involved in

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this process contribute to the development of novel pharmacological therapies.

Biography:

Jainne Martins Ferreira is the director of the science and health division of Neurogenesis Institute. As a postdoctoral student with François Noel at the Universidade Federal Rio de Janeiro she conducted a research about cardiotonic steroids and phenotype cell change. Previous she was a postdoctoral with Edward Ziff at the New York University conducting neuronal shape and studies. She joined Universidade Unigranrio School of Medicine, where she was Professor of Pharmaceutical Biotechnology and Neural Science and was an Investigator of the Translational Biomedicine Program.

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**Miroslav Radenković**

MD, PhD, Professor

Department of Pharmacology, Clinical Pharmacology and Toxicology

ACEIs/ARBs Prescribing in COVID-19 Patients: Role of ACE2 Receptors and Vascular Endothelium

ACE inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are frequently prescribed drugs in treatment of different cardiovascular pathologies, including hypertension and chronic heart failure. Still, it has been shown that chronic use of these drugs leads to increased expression of ACE2 receptors that are essential for binding of SARS-CoV-2 and further viral transmission to susceptible cells. One could suggest that by this action ACEIs/ARBs could actually further facilitate infective process and at the same time, deteriorate overall health. However, the effects of quoted drugs have been also tightly connected to protective actions against inflammatory and pro-coagulant effects of angiotensin II, which is extensively released especially in serious forms of COVID-19. There are emerging number of evidence that protective effects of ACEIs/ARBs are, at least in one part, strongly associated with functional preserving of blood vessels in SARS-CoV-2 affected tissues, in particular, of vascular endothelium. Accordingly, results of numerous experimental and clinical investigations clearly pointed to positive actions of ACEIs/ARBs in preserving vascular endothelium via pleiotropic vasodilating, antioxidant, anti-thrombotic, anti-proliferative, and all together, anti-atherosclerotic intracellular mechanisms. Thus, the current guidelines regarding appropriate ACEIs/ARBs use in COVID-19 patients are still under investigation, and this matter needs further clarification.

Biography:

Miroslav Radenković, MD, PhD, Professor, University of Belgrade, Faculty of Medicine, Department of Pharmacology, Clinical Pharmacology and Toxicology Education: 2019 Bioethics Masters Program, at Clarkson University and Icahn School of Medicine at Mount Sinai, NYC USA (in progress) Employment: 2016-present University of Belgrade, Faculty of Medicine - Full Professor, Pharmacology



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Evaluation of Nephroprotective Potential of Holarrhena Antidysenterica leaves in Experimental Diabetic Nephropathy in Rats

Deepti Bandawane

Dept of Pharmacology, Progressive Education Society's Modern College of Pharmacy, India.

Holarrhena antidysenterica L. (Apocynaceae) is a traditionally important Indian medicinal plant useful in different ailments such as amoebic dysentery, diarrhea, asthma and diabetes. The nephroprotective potential of the plant is however not scientifically evaluated. We have undertaken the present study with the aim to find out nephroprotective potential of ethyl acetate fraction of Holarrhena antidysenterica leaves (EAHA) in streptozotocin (STZ)-induced early diabetic nephropathy in experimental rats. Experimental diabetic nephropathy was induced in Wistar rats using single intraperitoneal injection of streptozotocin (65 mg/kg). Animals were divided in six groups (n=6) and treated with 100 mg/kg, 200 mg/kg & 400 mg/kg EAHA for 4 weeks. At the end of study period, fasting blood glucose, lipid profile, serum albumin, serum total protein, serum creatinine, blood urea nitrogen (BUN), glycosylated hemoglobin, and biomarkers of kidney oxidative stress were assessed. Urine was analyzed for the measurement of total protein, albumin, and creatinine clearance. Kidney sections were subjected to histopathological study. Daily oral administration of different doses of EAHA for 28 days normalized various biochemical, metabolic, and histopathological changes in the diabetic rats. EAHA significantly ($p<0.01$ and $p<0.05$) improved the glycemic status and renal function in diabetic rats as compared with diabetic control rats. Present study has revealed that EAHA prevented the progression of diabetic nephropathy in STZ-diabetic rats by improving the glucose homeostasis and by amelioration of oxidative stress in kidney.

Biography:

Dr. Deepti Bandawane, M.Pharm., Ph.D. Working as HOD & Professor, Dept. of Pharmacology at P.E.S. Modern College of Pharmacy, India. Receiver of 'Women Researcher Award' an International Scientist Award by VDGGOOD Professional Association, India during International Conference at Coimbatore on 4th & 5th July 2020.

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3,5-Bis[4-(diethoxymethyl)benzylidene]-1-methyl-piperidin-4-one, a Novel Curcumin Analogue, Inhibits Cellular and Humoral Immune Responses in Male Balb/c Mice

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Background: 3,5-Bis[4-(diethoxymethyl)benzylidene]-1-methyl-piperidin-4-one (BBP), a novel synthetic curcumin analogue has previously been shown to manifest potent immunosuppressive effects on the in vitro phagocytosis process of human neutrophils.

Objective: In the present study, BBP was investigated for its in vivo innate and adaptive immune responses mediated by different humoral and cellular immune factors.

Methods: Male Balb/c mice were orally fed with BBP (5, 10 and 20 mg/kg) for a period of 14 days and immunized with sheep red blood cells (sRBC) on day 0 for the determination of adaptive responses. The effects of BBP on phagocytosis process of neutrophils isolated from blood of treated/untreated animals were determined. The ceruloplasmin and lysozyme serum levels and myeloperoxidase (MPO) plasma level were also monitored. The mechanism was further explored by assessing its effects on the proliferation of T and B lymphocytes, T-lymphocytes subsets CD4⁺ and CD8⁺ and on the secretion of Th1/Th2 cytokines as well as serum immunoglobulins (IgG, IgM) and delayed type hypersensitivity (DTH) reaction.

Results: BBP showed a significant dose-dependent reduction on the migration of neutrophils, Mac-1 expression, phagocytic activity and reactive oxygen species (ROS) production. In comparison to the sensitized control group, a dose-dependent inhibition was observed on lymphocyte proliferation along with the downregulation of effector cells expression and release of cytokines. Moreover, a statistically significant decrease was perceived in serum levels of ceruloplasmin, lysozyme and immunoglobulins and MPO plasma level of BBP-treated mice. BBP also dose-dependently inhibited sheep red blood cells (sRBC)-induced swelling rate of mice paw in DTH.

Conclusion: These findings suggest the potential of BBP as a potent immunosuppressive agent.

Keywords: Curcumin Analogue, Innate Immune Response, Adaptive Immune Response, Phagocytosis, T-lymphocytes, Immunoglobulin

Biography:

Dr. Laiba Arshad is an Assistant Professor, Department of Pharmacy, Forman Christian College (A Chartered University), Lahore, Pakistan

PHARMACOLOGY & TOXICOLOGY

December 01-02, 2020 | Webinar

Food Chemicals Brings Toxic Effect on Health

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Manufacture of food and its conservation for long time may involve adding of chemicals. Hence, chemical constituents can play an important role in food manufacture and protection. The extracts in the food extend the shelf life of foods; standards, make food more gorgeous. Flavouring agents like aldehydes etc make food delicious. Unlike any other industry, agriculture is also a part of industry. The agriculture industry depends on greatly on large number of chemicals which may be toxic in nature. Some of these chemicals may get captivated by our body. The research on nerve cells has shown these chemicals to cause toxic effect on nerve cells. Accordingly, the use of chemicals involved in production, collecting processing, transport, packing, publicizing, and consumption creates poisonous effect on both human and ecology. Majority of the additives in the food may lead to headache, sickness, weakness, and difficulty in breathing. The research on nerve cells has shown these chemicals to cause toxic effect on nerve cells. Although the toxicants cannot be avoided, but the level can be reduced by adopting or making use of organic, sustainable, and less toxic options.

Keywords: Food, Chemicals

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Biological Treatment of Tuna Wash Processing Wastewater and Phytotoxicity Effect

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In recent years, there has been a rapid growth of the commercial fish industries across the world. Tuna industries demand large amounts of water for their processes and generate large volumes of wastewater enriched in organic matter that should be treated prior to release in the environment. Tuna wash processing wastewater (TWPW), if untreated or ineffectively treated, poses a threat to the aquatic environment. In this work, the TWPW was treated by using the yeast *Yarrowia lipolytica*. The biological treatment led to a reduction of chemical oxygen demand from 66 % to 75 %, total organic carbon from 70 % to 74 %, and total removal of phosphorus and nitrogen (100 %). Moreover, a useful *Y. lipolytica* biomass of 5 g L⁻¹ is produced after 7 days. The phytotoxicity assessment of the treated TWPW on fenugreek seeds showed promising results revealing the good performance of *Yarrowia* treatment in reducing the toxicity of this wastewater.

Keywords: Tuna Wash Processing Waste Water, *Yarrowia Lipolytica*, Phytotoxicity.

Biography:

Selma Hamimed is a Doctor/Laboratory of Biochemistry and Molecular Biology/Carthage University/Tunisia. She is a scientist loyal to microbial fermentation and industrial biotechnology/environmental sciences. Her research interests lie -amongst others- within biotechnological treatment and valorization of agro-industrial wastes into high-added value products (fuel, food, nutraceuticals, pharmaceuticals, biochemicals). Also, the application of nanotechnology for the valorization processes and formulation of enhanced biopolymers and green biocomposites for the biological treatment of toxic effluents.

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The Best Ester Substrate for The Studding Erythrocyte Cholinesterase Activity in a Baseline Independent Manner: Learning from Reaction Prediction

Sukhpreet Singh*

Rajasri Bhattacharyya, and Dibyajyoti Banerjee, Department of Experimental Medicine and Biotechnology, PGIMER, India

Erythrocyte cholinesterase (AChE) Is the gold standard biomarker of Organophosphorus pesticide poisoning. But this enzyme has significant inter as well as intra-individual variation. If a baseline free method is developed, then the problem of inter and intra-individual variation can be solved. Acetylthiocholine (ATCh) is the most popular substrate for AChE. In case reactivation-based methods are developed for AChE activity determination, then the baseline independent method can be designed. However, ATCh should not be an ideal substrate for it. The known reactivators of AChE (oximes) lyse ATCh. This is called oximolysis. To design baseline independent method, we believe that an ester substrate should be searched that will show minimal or no oximolysis but will be cleaved by AChE. Using tools of computational biology, we have searched for such a substrate after screening various ester substrates. It is observed that ester substrates behave different in-silico, which is discussed here.

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Ethnopharmacology of Processed Curcuma In the Prevention of Covid Related Symptoms

Joshi Venkata, N

India

Ayurveda has pluralistic formulations from basic herbal or food supplements been used for immune modulation. The processing techniques and adjuvants helps to boost such efficacy for immune system. Based on the traditional richness of knowledge and utility is the basis for such evaluation and results. The evidence is raised with the analogy of possible quality enhancement with compatibility and synergy building from fortified methods of formulations. In the presentation is to highlight the quality enhancement and immune modulation through ethnic background is highlighted

Biography:

Dr. Joshi Venkata, N is a Dean of Postgraduate Studies, Ayurveda Course ALN Rao Memorial Ayurveda College, Koppa, (India)

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Nanotechnology in Pharmacological use Pharmacokinetics and Oral Bioavailability of Omeprazole Nanosuspension after Oral Administration on Single- and Multiple-Dose Regimens to *Sprague-Dawley* Rats

Einas Majed Abu Arrah* and Toh Seok Ming

Universiti Sains Malaysia (USM), School of Pharmaceutical Sciences, Penang, Malaysia

Nanosuspension is a universal formulation method for poorly water-soluble drugs to overcome gastrointestinal barriers and improve oral bioavailability. This study was designed to quantitate and compare in the *Sprague-Dawley* rat the pharmacokinetics and oral bioavailability of nanosized omeprazole suspension after single-dose (20 mg) and multiple-dose (20 mg every 24 hr. for five doses) administrations in comparison with micronized omeprazole suspension. Plasma pharmacokinetic response of omeprazole was measured following intragastric gavage. Serial blood samples were collected and plasma drug concentrations were measured using High-Performance Liquid Chromatography. The time course of omeprazole in the plasma of all rats was best explained by a one-compartment model. In contrast to that observed with the micronized suspension, the nanosuspension had a faster onset of action with an improvement of oral absorption and bioavailability after single-dose and multiple-dose administration in rats. Administration of a multiple-dose of the omeprazole nanosuspension resulted in considerable increases in the maximum plasma levels of the drug compared to those observed after a single administration of omeprazole nanosuspension. The potentiating effects of the particle size reduction on omeprazole absorption persisted on multiple dosing.

Keywords: omeprazole nanosuspension, single and multiple doses, Pharmacokinetics, oral bioavailability, *Sprague-Dawley* Rats

Biography:

I've spent the 11 years learning everything there is to know about pharmacy from clinical to industrial. I'm currently applying this knowledge in my researches. I've held a number of scientific presentations and publish few articles. My research interests encompass the structure-bioavailability relationships exhibited by nanocomposites, and the selection of beneficial properties in polymers, nanoparticles, and their resulting composites. Specifically, I am driven to investigate the areas of drug nanocomposites, tuning and retention of unique nanoparticle physical properties in composites, and investigating its biological and physical activity.

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Suppression of Lncrna Malat1 by Betulinic Acid Inhibits Hepatocellular Carcinoma Progression by Targeting laps Via Mir-22-3p

Feiyu CHEN^{a*}, Zhangfeng ZHONG^a, Hor Yue TAN^a, Wei GUO^a, Cheng ZHANG^a,
Chien-Shan CHENG^a, Ning WANG^a, Junguo REN^b, Yibin FENG^a

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Betulinic acid (BA) is a natural product extracted from a broad range of medicinal and edible herbal plants. Previous studies showed that BA induces cell death in tumours derived from multiple tissues, however the underlying mechanism remains obscure. The present study aimed to study the effects of BA on autophagy and apoptosis of hepatocellular carcinoma (HCC). Human HCC cell lines and orthotopic HCC implanted mice were employed to examine the BA-induced tumor suppression; RT2 IncRNA PCR array and database analysis were used to explore the possible mechanisms; validation of pathways was performed using siRNA and miRNA inhibitors. The results indicated that BA regulated autophagy and induced apoptosis in HCC. The degradation of inhibitor of apoptosis proteins (IAPs), the conversion of LC3-I to LC3-II, as well as p62 accumulation were enhanced by BA, thereby suggesting that the down-regulation of IAPs and autophagic cell death are induced by BA. The addition of autophagy and lysosomal inhibitors indicated that BA induced autophagy-independent apoptosis via degradation of IAPs. Moreover, RT2 IncRNA PCR array and database analysis suggested that BA downregulated the levels of IncRNA MALAT1, which is considered to be an oncogene. Further investigations demonstrated that IncRNA MALAT1 functioned as a ceRNA (competing endogenous RNA) to contribute to BA-mediated degradation of IAPs by sponging miR-22-3p. Therefore, BA could be developed as a potential anti-cancer agent for HCC.

Biography:

Feiyu CHEN is a final year of PhD candidature at the School of Chinese Medicine, the University of Hong Kong. My work mainly focuses on Chinese Medicine and Hepatocellular carcinoma. I have 7 articles & interview papers published till now, which are 2 research articles (Clinical and Translational Medicine IF7.9, Frontiers in Pharmacology IF4.4); 3 review articles (Cancer Biology & Therapy IF: 3.38, Cancers IF6.1, Frontiers in Pharmacology IF4.4); two chapters for online open access books. And I have 2 articles that are under peer-review process.

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The Inhibitory Effect of Excisanin a on Breast Cancer Cell Growth is Associated With a Suppression in Integrin Signaling

Ibrahim G. Algayadh*

PhD, MSc, Rph, Saudi Food & Drug Authority (SFDA), Riyadh, Saudi Arabia

Breast cancer is the most common cancer and second leading cause of cancer death in Saudi women. Integrins are heterodimeric transmembrane receptors which mediate cell-adhesion. They are composed of α and β subunits which are bound noncovalently. The major function of integrin is to enhance attachment of cells to the extracellular matrix (ECM) and other cells, and mediate signal transduction between the extracellular matrix (ECM) and the cell. Integrin signaling has important role in cell survival, proliferation and cell cycle. Excisanin A is a diterpenoid compound purified from *Isodon macrocalyx* D. It is useful as a therapeutic agent for the treatment of inflammatory diseases, immunological diseases, and cancer. Exposure of breast cancer cells to excisanin A significantly inhibited cell migration and invasion and suppressed the mRNA and protein levels of matrix metalloproteinase-2 (MMP-2) and matrix metalloproteinase-9 (MMP-9) in a dose-dependent manner. Excisanin A efficiently abolished integrin $\beta 1$ expression and reduced the phosphorylation of the downstream kinases focal adhesion kinase (FAK) and Src. Additionally, Excisanin A inhibited the phosphorylation of phosphoinositide 3-kinase (PI3K), Akt and glycogen synthase kinase 3 beta (GSK3 β) and down-regulation of β -catenin expression. In summary, Excisanin A displays potent inhibitory effects on cancer cell growth through the targeting of integrin signaling, and shows great potential as a therapeutic approach in the treatment of breast cancer.

Keywords: integrin, breast cancer, Excisanin A.

Biography:

Dr. Ibrahim Algayadh is a scientific evaluation senior expert, Drug Sector, SFDA. Dr. Ibrahim Algayadh is a member in ICH S5 (R3) (Detection of toxicity to reproduction for human pharmaceuticals). He obtained his PhD in Pharmaceutical Sciences with specialization in Pharmacology and Toxicology from University of Louisiana at Monroe, USA in 2017. He previously obtained his Master degree in Toxicology from the University of Birmingham, UK in 2009. He also obtained his Bachelor degree in Pharmaceutical Sciences from School of Pharmacy, King Saud University. He has had a number of scientific articles published in peer-reviewed journals. Since joining the SFDA, he has been involved in the several scientific evaluation, strategic projects, consultations, SOPs, guidelines and regulations.

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Guessing game and poor quality teaching staffs study of less sunlight private pharmacy institution in Pune University

Rahul Hajare*

Fellow Indian Council of Medical Research

The researchers concluded that the finger have important implications for policy and prevention and should inform the creation of more effective sexual health education programs and interventions. Sex can accepted as non-negotiation strategies to sex. Hot have many perceptions. Black and whitish both can be hot. A HOT thinking is *higher-order thinking*, known as *higher order thinking* skills (HOTS). Old fat clothes women who find their mentally tiring are at increased risk of developing dull, a new study has found. The study suggests that mentally draining work such as teaching may increase the risk of dullness in women. According to the research, employers and women should be more aware of the potential health risks associated with mentally tiring work. Dullness is an increasingly prevalent disease that places a huge burden on patients and society and can lead to significant health problems including heart attacks, strokes, blindness, hair fall, mouth odour, under eye blackness, pelvis dislocation, one sided vagina, and kidney failure. Numerous factors can increase the risk of developing dullness including obesity, diet, exercise, smoking or a long term family history of the disease. In the study, Dr Rahul Hajare from the Indian Council of Medical Research Batch 2013 examined the effect of mentally tiring work on dullness incidence in over 20 women, during a 22- 32 year period. Approximately 75 per cent of the women were in the teaching profession and 24 per cent reported finding their work very mentally tiring at the beginning of the study due to lack of complete knowledge, The study has found that women were 21 per cent more likely to develop no happiness if they found their jobs mentally tiring at the start of the study. Skin turns out as baggy as their old “fat clothes. Under normal circumstances, seen no sexual desire or waiting for call.

Biography:

Dr. Rahul Hajare has been a hard worker all his academic life. After his Ph.D in Pharmacy from Bangalore which he completed with flying colours, he is fortunate to work NARI primer HIV research Institute to complete Post Doc of World Renowned Scientist Respected Dr. R.S.Paranjape., Retired Director & Scientist 'G' National AIDS Research Institute Pune. Dr. Rahul Hajare has Associate Professor of Medical Chemistry to Pune University (until 2020), he has serviced three times Associate Professor in Pharmaceutical Science and Analytical Science. Dr. Rahul Hajare now Principal of Ishwar Deshmukh Institute of Pharmacy affiliated to council f India.

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Determination and Evaluation of Crude Extracts of Batuan (*Garcinia Binucao* Linn. Family: clusiaceae) Fruits as Anti-Hyperlipidemic on High Cholesterol Diet - Induced Sprague Dawley Rats

Marin, Anthony R¹*, Bilbao, Plaudine Yvonne A., Koo, Ryson M., Lajo, Marie Alelli P. Manalo, Catalina Victoria M., Pascual, Sweet Mitzi M

¹St. Dominic College of Asia, Department of Pharmacy, Philippines

Hyperlipidemia is a major risk factor for heart disease, and this is the leading cause of death. Many people are suffering from hyperlipidemia and this ailment is one of the most common diseases in the Philippines. Herbal medicine is widely used throughout the world, especially in the Philippines, because it is cheap and readily available. Because of this, the researchers studied the anti-hyperlipidemic effect of Batuan (*Garcinia binucao* Linn.) to find a new source that can help treating hyperlipidemia. This study aims to determine and evaluate the antihyperlipidemic effect of Batuan fruits in Sprague Dawley rats. Extraction of Batuan was conducted by Maceration method using 95% Ethanol as solvent. A sample of 5 rats per group was employed in the study. Distilled water served as negative group, atorvastatin served as positive group and 50 mg/dL ad 100 mg/dL of Batuan extract served as treatment group. For Atorvastatin, the computed-value for HDL, LDL, TG, VLDL, and TC is less than .05 alpha level. This would mean that there is significant difference. Hence, Atorvastatin significant decrease the count LDL, TG, VLDL, and TC, and significantly increase the HDL count during post treatment. For 50 mg/dL Batuan extract, the computed p-value for HDL, LDL, TG, and TC is less than .05 alpha levels. This would mean that there is significant difference. Hence, 50 mg/dL Batuan extract significantly decrease the LDL, TG, and TC and significantly increase the HDL count during post treatment. For 100 mg/dL Batuan extract, the computed p-value for HDL, LDL, TG, and TC is less than .05 alpha level. This would mean that there is significant difference. Hence, 100 mg/dL Batuan extract significantly decrease the LDL, TG, and TC and significantly increase the HDL count during post treatment.

Keywords: Batuan as Antihyperlipidemic, Lipidemic, Batuan Plants, Cholesterol, Atorvastatin

Biography:

Prof. Anthony Rios Marin is a Program Head, BS Pharmacy Department of Pharmacy School of Health Science Professions, St. Dominic College of Asia, Philippines

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December 01-02, 2020 | Webinar

Evaluation of the Efficacy and Safety of Cinchona and A Phytomedicament “Acar” In Comparison with Hydroxychloroquine In Adult Patients with Covid-19 without Symptoms

Mamadou Saliou Sow^{*1,2}, Fodé Bangaly Sako^{1,2}, Mohamed Sahar Traoré^{1,3}, Alioune Camara^{1,4}, Elhadj Saidou Baldé^{1,3}, Fodé Amara Traoré^{1,2}, Thierno Mamadou Tounkara^{1,5}, Mohamed Maciré Soumah^{1,3}, Mory Chérif¹, Kadiatou Diallo^{1,6}, Aïssatou Taran Diallo^{1,7}, Mohamed Cissé^{1,3}, Mamadou Aliou Baldé^{1,3} et équipe de recherche des phytomédicaments de Guinée (Alpha Oumar Baldé, Souleymane Taran Diallo, Mariama Diouldé Sall, Fatoumata Bah, Mamadou Alpha Diallo, Mamadou Samba Dramé, Djessona Dioubaté, Kalil Polia Camara, Mohamed Kerfalla Camara, Ténè Woulen Keita, Fodé Bangaly Magassouba, Saïdou Traoré, Agnès Sangaré, Kalil Sylla

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⁵Service Dermatologie-vénéréologie de l'Hôpital National Donka, ⁶Service de Gastro-entérologie de l'Hôpital National Donka, ⁷Service de Chirurgie générale de l'Hôpital National Ignace Deen

Objective: to evaluate the efficacy and tolerance of Phytomedicines from the pharmacopoeia and traditional Guinean medicine.

Patients and methods : These were adult patients (age ≥ 18 years) with a COVID-19 confirmed by PCR (Polymerase Chain Reaction) without symptoms. As an “add on” to Azithromycin, Quinquina-based phytomedicines, arm 2 (“CILE”) and herbal combination, arm 3 (“ACAR”) were compared to Hydroxychloroquine, arm 1. The primary endpoint was the virological clearance of nasopharyngeal secretion samples at days 3, 6 and 14. Data were entered and processed using STAT software.

Results : Two hundred and thirty-one patients were included at three COVID-19 management sites in Conakry. Patients' socio-demographic data were comparable in all three arms at admission. The mean age was 35.4 ± 11.6 years for arm 1, 35.8 ± 12.3 years for arm 2 and 36.6 ± 12.7 years for arm 3. We noted the appearance of clinical signs between D1 and D3 on 48 occasions. No major side effects were noted in all three arms. The mean length of stay was 4.9 ± 5.1 days overall. Of the 231 patients included, a negative PCR at D3 was noted in 157 patients : 70.1% ($n=54/77$) for arm 1, 67.5% ($n= 52/77$) for arm 2 and 66.2% ($n= 51/77$) for arm 3. At D6, 208 (90.04%) patients had a negative PCR, i.e. 91% ($70/77$), 89.61% ($69/77$), and 88% ($68/77$) respectively for arms 1, 2 and 3. At D14, the PCR was negative for 221/231 patients (95.67%).

Conclusion the therapeutic effect of the tested phytomedicines is not inferior to that of hydroxychloroquine. The phyto drugs are as well tolerated as the standard treatment Guinea. A phase III clinical trial is in prospect for confirmation of the effects of the phytomedicines.

Keywords : Phytomedicines, Hydroxychloroquine, Covid-19, traditional medicine, Conakry

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December 01-02, 2020 | Webinar

Adult Dental Pulp Mscs: Safety and Efficacy in Chemically-Induced Hyperglycemic Rats

Shivani Desai*, Abhishek Kuwar, Ramesh Bhonde, Avinash Sanap, Avinash Kharat

Dr. D. Y. Patil Institute of Pharmaceutical Sciences and Research, Pune, India

The aim of the present study was to compare the effects of adult dental pulp mesenchymal stem cells (DPSCs) transplantation into the diabetic rats with hyperglycemia. DPSCs were isolated and identified by flow cytometry. Rats with streptozocin induced diabetes to obtain a rat model of hyperglycemia, followed by transplantation of DPSCs into the intramuscularly. After starting the treatment, the blood glucose and body weight of animals were measured, the section of animal tissue were observed following hematoxylin and eosin (H&E) staining for histopathological significance. The cellular ultrastructure was examined by transmission electron microscopy. The result of blood glucose and body weight was demonstrated that there were no significant differences in blood glucose levels and body weight were observed. The H&E staining results demonstrated that the DPSCs have effect like regeneration of the pancreas. Transmission electron microscopy examination revealed that the ultrastructure of the tissues in the DPSCs treated group was not show any abnormality of pathological significance compared with that in the diabetic model group. In conclusion, DPSCs were found to be safe in the hyperglycemia.

Keywords: Mesenchymal Stem Cells, Adult dental pulp stem cells (DPSCs), Hyperglycemia, Safety

Biography:

I am a Clinical Pharmacist with PhD in Pharmaceutical Sciences. Along with academic profile I am involved in various preclinical and clinical projects. Currently I am working on projects such as development of vaccine for type 1 diabetes mellitus, clinical trial for anti-obesity formulation, clinical evaluation of possible causes and complications of type 1 diabetes mellitus, pre-clinical study on application of stem cells in diabetes mellitus and in diabetic wound, pre-clinical study on application of stem cells in pancreatic transplantation in type 1 diabetes mellitus. I have publications in national and international journals indexed in Scopus and Web of Science.

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Identification of the 3,4-Dihydro-2H,6H-Pyrimido[1,2-c][1,3]Benzothiazine-6-imine Derivatives as Novel selective Inhibitors of the *Plasmodium falciparum* Dihydroorotate Dehydrogenase

Endah Dwi Hartuti^{1,2*}, Daniel Ken Inaoka^{3,4,5}, Takaya Sakura^{3,4}, Mohammed S. O. Tagod⁴, Xinying Wang³, Kota Mochizuki¹, Rajib Acharjee¹, Yuichi Matsuo⁴, Mihoko Mori⁷, Danang Waluyo², Kazuro Shiomi⁷, Tomoyoshi Nozaki⁵, Shinjiro Hamano⁸ and Kiyoshi Kita^{4,5,6}

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⁸Department of Parasitology, Institute of Tropical Medicine (NEKKEN), Nagasaki University, Japan.

Plasmodium falciparum is an apicomplexan parasite that is responsible for the development of malaria. The parasite has evolved resistance to conventional antimalarial drugs used in many endemic areas rendering development of novel antimalarial drugs as an urgent issue. Mitochondria carry out biochemical functions essential for almost all eukaryotic cells such as homeostasis calcium, signaling for cell death and survival also ATP production. In addition to that, mitochondria are also important organelle for de-novo pyrimidine biosynthesis. Studies of antimalarial drug target identified dihydroorotate dehydrogenase (DHODH) as potential drug target which involve in the fourth step of pyrimidine biosynthesis. PfDHODH is belong to Family 2 enzyme that catalyze the oxidation of dihydroorotate to orotate and the electrons are transferred to ubiquinone in the respiratory mitochondrial chain via the involvement of cofactor, flavin mononucleotide (FMN). The inhibitor binding site of *P. falciparum* DHODH is known to be structurally divergent from the mammalian orthologue. Its characteristic and functionalities allow development of pathogen-specific inhibitors. In this study, we screened around 40,000 compounds from Kyoto University's library in 384-well plates against recombinant PfDHODH. The screening identified PD 404182 and its derivatives as rPfDHODH inhibitors and among them ten compounds showed IC₅₀ of under 1 μ M. The average Z'-factor was 0.875 ± 0.088 and the coefficients of variation was 2.38% indicating excellent performance of the screening systems. Finally, PD 404182 and its derivative also inhibited the growth of *P. falciparum* 3D7, providing new starting points for antimalarial drug development.

Keywords: *Plasmodium falciparum*, dihydroorotate dehydrogenase, inhibitors

Biography:

Endah Dwi Hartuti, Apt, M.Biomed is a PhD student, Graduate School of Biomedical Science, Nagasaki University, Japan

NOTE:



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