Exhibitor Hosted Session
November 01, 2017

Toxicology Conference 2017

International Conference on

Toxicology and Pharmacology

November 01-02, 2017 | Toronto, Canada

Corina T Bot

Nanion Technologies, Germany

Short and long-term cytotoxicity investigations in stem cells for primary and secondary assays with an all- inclusive approach

In recent years, human stem cell-derived cardiomyocytes (hiPSC-CMs) have proven to represent a relevant human *in-vitro* system for modeling and interrogating complex biological processes, phenotypic profiles and disease models. Chip-based approaches allow parallel patch clamp recordings without compromising data quality or technical sophistication. We present high-throughput ion channel recordings in hiPSC-CMs using Nanion's automated patch clamping systems. The CardioExcyte 96 is a hybrid screening instrument that combines impedance with MEA-like extracellular field potential (EFP) recordings. In the light of the new Comprehensive . Proarrhythmia Assay (CiPA), a FDA directed initiative to improve guidelines and standardize assays and protocols, the use of hiPSC-CMs may become critical in determining the proarrhythmic risk of potential drug candidates. In accordance with the CiPA guidelines, we present pharmacological investigations of short- and long-term effects of compounds from each risk category, in hiPSC-CMs. This approach strengthens the importance of testing compounds in assays complementary to patch clamp electrophysiology, to provide a more complete safety profile.

Speaker Biography

Corina T Bot obtained her PhD in Applied Physics from New Jersey Institute of Technology in 2010. Next, she worked for two years as a Post-doctoral Associate in Cardiology, at Cornell University, Weill Cornell Medical College. In her current position as a Senior Scientist at Nanion Technologies, she provides technical and scientific support for cell-based electrophysiology and toxicology assays, and automated patch clamp screening. Together with her colleagues at Nanion, she is participating in the FDA-directed Comprehensive *in vitro* Proarrhythmia Assay (CiPA) initiative, which aims to replace the preclinical hERG current assay required under the ICH S7B safety pharmacology guidelines and clinical TQT study.

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Scientific Tracks & Abstracts
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Endogenous negative regulators of inflammation preserve neuronal survival

Denis Gris
University of Sherbrooke, Canada

Cyanotoxins have been shown to be highly toxic for mammalian cells, including brain cells. However, little is known about their effect on inflammatory pathways. Our study investigated whether mammalian brain and immune cells can be a target of certain cyanotoxins, at doses approximating those in the guideline levels for drinking water. We examined the effects on cellular viability, apoptosis, and inflammation signaling of several toxins on murine macrophage-like RAW264.7, microglial BV-2, and neuroblastoma N2a cell lines. We have tested cylindrospermopsin (CYN), microcystin-LR (MC-LR), and anatoxin-a (ATXa), individually as well as in mixture. Searching into protective mechanism against cyanotoxins, we found that Nlrx1, a protein localized to mitochondria, ameliorates toxin effects. Decreased expression of Nlrx1 correlated with increased vulnerability of all cell types to toxin exposure. Our results demonstrate that CYN, MC-LR, and ATX-a, at low doses individually and in mixture, have potent effect inducing apoptosis and inflammation. Further research of the neuroinflammatory effects of these compounds *in-vivo* is needed to improve safety limit levels for cyanotoxins in drinking water and food.

Speaker Biography

Denis Gris has completed his PhD in the Neuroscience program at the Western University of Ontario and moved to the University of North Carolina at Chapel Hill where he studied mechanism of immune responses. His laboratory studies a role of inflammation in the development and progression of neurodegenerative disorders and using *in-vitro* and *in-vivo* models, he aims to uncover novel endogenous pathways that limit neuroinflammation. At his lab, with his co-workers, they pair molecular work with latest state-of-the-art automated behavioral assessment technology, to study how inflammation changes CNS function.

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A risk of exposure to noise and air pollution to human health

Olga Anne (Belous) and **Agne Stoniene**
Klaipeda University, Lithuania

The World Health Organization (WHO) pays attention to the evidence highlighting the necessity of sustainable approach of health, environment and transport interaction. Frequently, the influence of physical or chemical pollution that are associated with a certain risk to human health, are evaluated separately. The cumulative effect of both could have significant impact to human health, for instance, to cause cardiovascular diseases. The intention of the study is to determine the risk of the cumulative effect of city traffic noise and air pollution on population health and to propose measures to reduce the risk. The measurements of the transport equivalent noise level, particulate matter (PM_{10}) and nitrogen dioxide (NO_2) emissions were carried out at the most noisy and polluted areas of the city. At the same time the citizens opinion poll regarding their health state was organized. The evaluation of noise levels as well as certain pollutants concentrations in the ambient air and their possible cumulative risk to human health was fulfilled. The suggestions on how to reduce the negative health risk of transport noise and air pollution were proposed. The results of the measurements performed and the questionnaire survey suggest that the inhabitants of the city are exposed to the interaction of noise and certain air pollutants. The assessments of the state of the health submitted by the respondents were correct and in accordance with vehicles noise and outdoor air pollution levels. As a consequence, people are at risk of cardiovascular and respiratory diseases. The most sensitive population group of transport impact caused by noise and air pollution is elderly people.

Speaker Biography

Olga Anne has completed her PhD from Moscow Chemical Technological University, Russia. She is the Senior Researcher/Professor of Klaipeda University, Lithuania. She has over 60 publications in pre-reviewed journals and 17 of them are in *ISI WOS journals* that have been cited over 45 times.

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Notes:

Molecular targeting of ERKs-RSK2 signaling axis in human cancer

Yong-Yeon Cho and **Cheol-Jung Lee**
The Catholic University of Korea, Korea

Receptor tyrosine kinases (RTKs) which are activated by diverse stimuli, such as growth factors, cytokines and environmental stresses, play a key role in cell proliferation, transformation and cancer development in humans. Since constitutive active mutations in Ras and Raf are frequently observed with high percentage in many solid tumors, including colon, pancreas, ovarian, melanoma, non-small cell lung and other cancers, Ras-mediated Rafs/MEK/ERKs/RSK2 signaling axis plays a key role in the regulation of cell proliferation, transformation and cancer development. Thus, Ras/Rafs/MEKs/ERKs/RSKs signaling pathway has become an important target to develop/identify chemopreventive and therapeutic agents. Recently, our results demonstrated that RSK2, a downstream kinase of ERKs, is an important proof-of-concept on the human cancer development. Ectopic expression of RSK2 induced anchorage-independent cell transformation without stimulation of tumor promoters such as epidermal growth factor. Moreover, human skin cancer tissue array demonstrated that total- and phospho-RSK2 protein levels were higher in skin cancer tissues compared with normal skin tissues. Utilizing cutting edge molecular and computational research tools, we provided evidences that kaempferol and eriodictyol were natural compounds which target and inhibit RSK2 activity. Moreover, we found that magnolin, a natural compound abundantly found in magnolia flos, targeted ERK1 and ERK2 and inhibited ERK1 and ERK2's activities with 68 nM and 16.5 nM of IC_{50} values. Moreover, magnolin suppressed cell migration and invasion in cancer cells by inhibition of epithelial-to-mesenchymal transition of cancer cells. Taken together, our results provide strong evidences that ERKs and RSK2 are key kinases regulating cell proliferation and transformation, and are important targets to develop/identify small molecules as chemopreventive and/or therapeutic agents.

Speaker Biography

Yong-Yeon Cho, PhD, is an Associate Professor and Director for Integrated Research Institute of Pharmacutical Sciences at the College of Pharmacy, The Catholic University of Korea. He earned his PhD degree at the Tohoku University (Applied Genetic Engineering) under the supervision of Professor Tokuo T Yamamoto in Sendai, Japan in 2000. He then joined Zigang Dong as a Post-Doc at the Hormel Institute, University of Minnesota, in Dec-2001. He brought with him his expertise in Molecular Biology and Genetic Engineering, which was integral to the research of protein-protein interactions, signaling networks and molecular targeting of small molecules. Based on his scientific achievements, he became Research Assistant Professor at the Hormel Institute, University of Minnesota in 2005. His efforts resulted in the breakthrough that the post-translational modification of stem cell factors plays an important role to regulate stemness of ES cells and reprogramming efficiency. He came back and started a new endeavor in Korea in 2011. Currently, he continues his research on molecular mechanisms of novel signaling pathways regulating protein stability regulation in cancer development and chemoresistance.

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Functionalization of ZnO nanoparticles by 3-mercaptopropionic acid for aqueous curcumin delivery: Synthesis, characterization and anticancer assessment

M Reza Khorramizadeh[1], Seyed-Behnam Ghaffari[2], Mohammad-Hossein Sarrafzadeh[2], Zahra Fakhroueian[2] and **Shadab Shahriari[1]**

[1]Tehran University of Medical Sciences, Iran

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Inherent biocompatibility and stability of zinc oxide nanoparticles (ZnO-NPs) and their biomedical potentials make them an emerging candidate for drug delivery. The aim of this study was to develop and assess a simple procedure for surface functionalization of ZnO-NPs by 3-mercaptopropionic acid (MPA) for water-soluble curcumin delivery. Carboxyl-terminated ZnO nanoparticles were successfully made using $ZnCl_2$ and NaOH in the presence of MPA. The functional groups were activated by 1, 1'-Carbonyldiimidazole (CDI) and the curcumin bonding was carried out at room temperature for 24 h. The core-shell nanocomposite had a significant better solubility versus free curcumin, as characterized by XRD, FTIR, UV-Vis spectrophotometry, DLS, and TEM, $p<0.005$. In addition, MTT cytotoxicity assessment on MDA-MB-231 breast cancer cells revealed a drop of IC_{50} values from 5 µg/mL to 3.3 µg/mL for free curcumin and ZnO-MPA-curcumin complex, respectively. This result showed an augmented cancer-inhibitory effect of nanoconjugate complex. In conclusion, the presented improved solubility and elevated functionality of novel ZnO-MPA-curcumin nanoformula is promising, and could be considered for new therapeutic endeavors.

Speaker Biography

M Reza Khorramizadeh, is a full Professor at Tehran University of Medical Sciences (TUMS), directs Biosensor Research Center and newly instituted Zebra Fish Core Lab at Endocrinology and Metabolic Molecular-Cellular Sciences Institute. Concurrently, he is a 2nd affiliation to the Dept. of Medical Biotechnology, School of Advanced Technology in Medicine, TUMS.

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Notes:

Novel toxicity related to nanomaterials? Silica nanoparticles cause pleural effusion and pericardial effusion in workers and in rats

Yuguo Song
Capital Medical University, China

Nanomaterials introduce novel risk factors and potentially lead to novel hazards within the workplace or through environmental contamination. Here, we introduce our study in the nanoexposed workers and animal experiments. Further information on the novel toxicity related to the silica nanoparticles was collected and the potential mechanisms were discussed. With the rapid development of nanotechnology and the extensive use of nanoproducts, the potential hazards of nanomaterials to the environment and human health were widely concerned. Nanomaterials introduce novel risk factors and potentially lead to novel hazards within the workplace or through environmental contamination. *In vitro* and *in vivo* studies show that the toxicities nanomaterials posed include damage to lungs, heart, liver, kidney and nerve, as well as reproductive and immune systems and they also have carcinogenicity. Additionally, some studies reported the specific toxicity of nanomaterials which appears due to their unique physicochemical properties. However, it is still controversy in regarding to the nano-specific toxicity, and some scientists regard that there is no evidence of novel 'nano-specific hazard' comparing to micro –materials. We previously reported that a group of patients exposed to nanomaterials presented with an unusual disease with pleural and pericardial effusion, pulmonary fibrosis and granuloma. And our further rodent study shows that silica nanoparticles that were isolated in patients can also cause pleural effusion and pericardial effusion- a rare and unusual symptom- which may be the novel toxicity related to nanomaterials. Here, we introduce our study in the nanoexposed workers and animal experiment, further information on the novel toxicity related to the silica nanoparticles was collected and the potential mechanisms will be discussed.

Speaker Biography

Yuguo Song works as a Chief-physician and the Deputy Director at the Department of Occupational Medicine & Clinical Toxicology, Beijing Chaoyang Hospital, Capital Medical University (Beijing, China). He received his BS degree in Clinical Medicine from the University of Tsingdao Medical College, Shandong Province in 1990, and then he got his MD and PhD degree in Capital Medical University. He is the recipient of several research achievement awards including Wu Zhizhong Prize in Occupational Medicine (China) and International Travel Award from the American Academy of Clinical Toxicology. He worked as a Visiting Scholar in 2010 at West Virginia University, USA. His research focus is on occupational lung disease, clinical toxicology and nanotoxicology.

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The connection of changed cholinergic receptors with the deficit of learning and memory of rats with chronic fluorosis

Zhi-Zhong Guan, Yang-Ting Dong, Yan-Jie Liu, Chuan-Zhi Gui, Qin Gao and **Na Wei**
Guizhou Medical University, China

In order to reveal the mechanism of decreased learning ability and memory induced by chronic fluorosis, nicotinic acetylcholine receptors (nAChRs) and muscarinic acetylcholine receptors (mAChRs), cholinesterase (ChE) activity and oxidative stress were investigated using rats with chronic fluorosis. Spatial learning and memory of the rats were evaluated by Morris Water Maze test. The expressions of nAChRs and mAChRs at protein and mRNA levels were detected by Western blotting and real-time PCR, respectively. ChE activity and the level of oxidative stress were determined by chemical colorimetry. The results showed that the learning and memory capacity in rats with chronic fluorosis was decreased. In the brain tissues from the rats with fluorosis as compared to controls, the protein expressions of nAChR and mAChR subunits were lower, and the corresponding mRNAs of these receptor subunits changed; the activities of acetylcholinesterase (AChE) were reduced, but no change of butyrylcholinesterase (BuChE); the increased MDA content and the decreased activities of SOD and GSH-px were found. The results indicated that the deficit of learning and memory of the rats with chronic fluorosis may be in mechanism correlated with the inhibited expression of cholinergic system and the increased level of oxidative stress.

Speaker Biography

Zhi-Zhong Guan completed his PhD from Karolinska Institutet, Sweden in 1997. He is the Director of the Key Lab of the Endemic and Ethnic Diseases in Education Ministry of China. He has published more than 400 papers (including more than 100 SCI collected papers) in peer-reviewed journals and has been serving as an Editorial Board Member or reviewer of several journals.

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Workshop Session
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Nanion Technologies, Germany

Impedance and extracellular field potential for cardiac safety assays: A combined approach for non-invasive screening of iPS cells

The CardioExcyte 96 is a hybrid screening instrument that combines impedance with MEA-like extracellular field potential (EFP) recordings. Changes in the impedance signal indicate effects on cell contractility and overall shape, whereas the field potential parameters provide information about the electrophysiological activity of the beating network of cells. The ongoing Comprehensive *in-vitro* Proarrhythmia Assay (CiPA) is a FDA directed initiative to improve guidelines and standardize assays for determining the proarrhythmic risk of potential drug candidates. In agreement with the CiPA initiative, standard protocols and SOPs were created for the CardioExcyte96, as well as automated data analysis on required endpoints. Workshop presents the workflow of utilizing the CardioExcyte96 for the assessment of acute/chronic cardiotoxicity in cultured iPSC cardiomyocytes. Cytotoxic responses of cell monolayers involve metabolic or biochemical changes that affect the morphology of the cells, or reduce their overall viability. In that regard, effects of reference compounds tested for long-term cytotoxicity in hepatocyte-like cells will be presented.

Speaker Biography

Corina T Bot obtained her PhD in Applied Physics from New Jersey Institute of Technology in 2010. Next, she worked for two years as a Post-doctoral Associate in Cardiology, at Cornell University, Weill Cornell Medical College. In her current position as a Senior Scientist at Nanion Technologies, she provides technical and scientific support for cell-based electrophysiology and toxicology assays, and automated patch clamp screening. Together with her colleagues at Nanion, she is participating in the FDA-directed Comprehensive *in vitro* Proarrhythmia Assay (CiPA) initiative, which aims to replace the preclinical hERG current assay required under the ICH S7B safety pharmacology guidelines and clinical TQT study.

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A high throughput targeted and non-targeted method for the analysis of microcystins and anatoxin-A using on-line solid phase extraction coupled to liquid chromatography - quadrupole time-of-flight high resolution mass spectrometry

Xavier Ortiz
Ontario Ministry of the Environment and Climate Change, Canada

Microcystins are cyclic heptapeptide hepatotoxins produced by cyanobacteria in freshwater. Sample preparation for the analysis of these cyanotoxins in water from algal blooms can take up to several days due to the matrix complexity and the low detection limits required complying with current legislation. Moreover, there is a large number of unknown microcystins that could potentially exist in the environment resulting from different amino acid substitutions into the microcystin skeletal structure. To tackle these problems, the present study involved the development of a high throughput method based on on-line solid phase extraction coupled to liquid chromatography that can provide quantitative results for 12 microcystin variants (LR, YR, RR, HtyR, HilR, WR, LW, LA, LF, LY, Dha7-LR and Dha7-RR) and anatoxin-A in less than three hours with detection limits between 0.004-0.01 µgL-1 and uncertainty between 4-14%. Data dependent acquisition was employed for the non-targeted analysis of these cyanotoxins. Filtering the data based on structure diagnostic fragments, two unknown microcystin variants not previously reported in the literature were detected. The structures Leu1-microcystin-Met(O)R and Leu1-microcystin-LY were fully characterized by accurate mass measurement, collision induced dissociation and fragmentation prediction software.

Speaker Biography

Xavier Ortiz obtained his PhD degree at IQS-Barcelona (Spain), where he developed methods for the analysis of Persistent Organic Pollutants in food using GC-HRMS technology. Before coming to Canada, he worked in the pharmaceutical and biotechnology private sectors as Analytical Lab Manager; characterizing, isolating and purifying natural products from microalgae by preparative LC. Currently, he is a Research Scientist at the Ontario Ministry of the Environment and Climate Change, developing new methods for the analysis of emerging pollutants in the Canadian Environment using chromatography and mass spectrometry. He is the Ministry's Lead Scientist in cyanotoxins analysis, specializing in lab automation to increase productivity and non-targeted analysis of previously unknown toxins.

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Developing new approaches to the health hazard assessment of potent pharmaceuticals

Tracy A Kimmel
SafeBridge Consultants, Inc., Canada

The current approach to setting "safe" levels of exposure to potent pharmaceutical compounds has remained fundamentally unchanged for over 50 years. This approach has been applied to both worker setting (through the setting of Occupational Exposure Limits) and, more recently, patient and/or product safety (through the setting of Permitted Daily Exposures). New developments in pharmaceutical technology (i.e., antibody-drug conjugates, nanodrugs, viral vectors and other biologicals, and emerging immunotherapy targets) have combined with ever-increasing drug potency present challenges to the paradigm of hazard assessment, and have spurred advances and adaptations by which robust evaluations of these compounds can be performed. The purpose of this presentation is to deliver an overview of the hazard assessment process and its applicability to both work and patient/product safety, which will include a description of what constitutes a "potent" pharmaceutical agent. Application of hazard assessment methodologies to novel drug candidates and drug delivery technologies, which stretch the boundaries of established approaches to hazard assessment, will then be discussed.

Speaker Biography

Tracy A Kimmel has received her PhD in Environmental Health Sciences from New York University, and is a Diplomate of the American Board of Toxicology. She has almost 25 years' experience in the pharmaceuticals industry, including 12 years working with Corporate EH&S groups. She is currently Senior Manager of Toxicology at SafeBridge Consultants, Inc. Her primary responsibilities include performing health hazard assessments of pharmaceutical and industrial compounds, predicting the toxicity of compounds using computational modeling software and qualitative analyses, evaluation of pharmaceutical impurities and synthetic intermediates, and assisting with environmental risk assessments. She is a former Chair of the Occupational Alliance for Risk Science (OARS) Workplace Environmental Exposure Level (WEEL) Committee, and now serves on the ACGIH Threshold Limit Value (TLV®) Committee. She has contributed to peer-reviewed journal articles and publications, has prepared white papers on occupational hazard assessment, and has delivered presentations and workshops at worldwide locations.

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Evaluating the abuse potential of CNS active drugs: Regulatory and methodological considerations

Beatrice Setnik[1, 2]
[1]INC Research, Canada
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Prescription drug abuse continues to be a great concern and regulatory agencies such as the FDA and Health Canada require abuse potential evaluation to inform appropriate drug scheduling for novel CNS-active drugs at the time of drug approval. One of the required studies includes the human abuse potential study (HAP). HAP studies are a type of clinical study evaluating subjective and objective drug effects related to abuse potential and drug impairing effects. The preferred design is a randomized, double-blind, placebo- and positive-controlled crossover study. The studies are generally conducted in drug-experienced, non-dependent recreational drug users who have a past and recent history of using a drug in the pharmaceutical class of the test drug. Generally, these studies are considerably distinct compared to healthy volunteer and patient studies, and host their own complexities and challenges. The drug using population represents a unique subgroup requiring adaptions to clinical trial methodology. Challenges with these populations include, but are not limited to, compliance with restrictions around concomitant medication and drug use, risk-taking behavior, and prior addictive disorders. The population needs to be carefully selected and screened to ensure that safety is not compromised, eligibility requirements are met, appropriate discrimination between the active control versus placebo is established, and that subjects are able to comply with the study requirements. Furthermore, a population using drugs by a specific route (e.g. intranasal, intravenous) may be needed if the clinical trial intends to study unintended routes of administration, as is often the case in studies evaluating abuse-deterrent formulations. Understanding the profile and nature of the population and the study requirements ensures appropriate rigidity in the methods and conduct of such studies. This session will provide an overview of the key regulatory and clinical methodological considerations in conducting HAP studies.

Speaker Biography

Beatrice Setnik has been working in the area of CNS research, clinical drug development and abuse potential assessment for over 16 years and is an expert in the area of abuse liability evaluation. She is currently the Vice President of Scientific and Medical Affairs at INC Early Phase and an Adjunct Professor with the Department of Pharmacology and Toxicology at the University of Toronto. She earned her Doctorate degree in Pharmacology and the Collaborative Program in Neuroscience from the University of Toronto in 2005.

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Video Presentations

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An analytical study of deaths due to poisoning in Visakhapatnam

Rama Krishna Pedada, V Chandra Sekhar, P Venkata Ramana Rao and **N Dev Chand**
Andhra Medical College- King George Hospital, India

Objective: To determine and classify the various types of poisoning deaths as seen at Andhra Medical College Mortuary, Visakhapatnam city.

Materials & Methods: This is a retrospective study of all the deaths due to poisoning seen in the Department of Forensic Medicine and Toxicology, Andhra Medical College, Visakhapatnam City over a 15-year period (January 2001-December 2015) as recorded in the autopsy registers and postmortem reports of the department.

Observations: Poisoning is one of the commonest methods of committing suicide especially in developing countries like India. A total of 22475 autopsies were done during the period. 2074 cases representing 9.23% of all bodies received by the mortuary were deaths due to poisoning. Organophosphate compounds were the most commonly 78.98% abused substance. The common motive of poisoning was suicidal 93.43% with male to female ratio 6.69:1. Peak incidence was observed in the age group 21-40 years. Type of poison consumed, socioeconomic status and place of household are also ascertained.

Conclusion: This study shows the pattern of poisoning deaths in Visakhapatnam and this preliminary data will provide a baseline for future research and help in formulating policies to prevent deaths due to poisoning.

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Ameliorative potential of Eugenol and Carvacrol in cobalt mediated hypercontraction in isolated Wistar rat aorta

Shahnawaz Ahmad Wani and **Seemi Farhat Basir**
Jamia Millia Islamia, India

Cobalt is a very important element that is naturally present in biochemically important compounds like cyanocobalamin (Vit B_{12}). But occupational exposure of cobalt is reported to cause various diseases like lung cancer, cardiovascular diseases like cardiomyopathy and gastrointestinal diseases. Cobalt is reported to augment vascular contractility in spontaneously hypertensive rats. So, we have planned this study to check contractile effect of cobalt in toxic range on Wistar rat aortic rings, and to study the ameliorative potential of eugenol and carvacrol which are plant derived terpenoids and possess antioxidant activities using organ bath system (Ad instruments). In our study, a hyper-contractile response was seen at all the various concentrations of cobalt used, i.e. 800 nM, 10 µM, and 50 µM and the hypercontractile response in case of cobalt incubated aortic rings were 132%, 128%, 108% respectively with respect to control taken as 100% with Phenylephrine induced contraction. Eugenol and carvacrol could act as possible ameliorators of hypercontraction. We have noticed that at saturating concentration of 100 µM eugenol and 10 µM carvacrol caused 38% and 42% relaxation in cobalt unexposed aortic rings; while 40% and 48% relaxation was observed when cobalt exposed aortic rings were co-incubated with eugenol and carvacrol. In our study, we have found that the relaxation caused by both the natural compounds is due to the quenching of ROS and by enhancing nitric oxide release from endothelium of aorta. To conclude, acute exposure of cobalt to aortic rings causes increase in hypercontractile response by generating oxidative stress, which is effectively lessened by eugenol and carvacrol.

Speaker Biography

Shahnawaz Ahmad Wani did his MSc Biochemistry from Jamia Millia Islamia (JMI), New Delhi India. He is pursuing PhD from Department of Bioscience, JMI and is working on topic titled as "Effect of Metal Pollutants on Cardiovascular System". He has presented four conference paper in various national and international seminars. He has one publication on titled mechanism of flavonoids in smooth muscle relaxation.

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Safety and toxicity evaluations of *Xanthium strumarium* Linn

Bhanu P S Sagar and **Srishti Singh**
IEC College of Engineering & Technology- IEC Group of Institutions, India

Xanthium strumarium L. is poisonous to mammals due its toxic principle which is a diterpenoid glycoside i.e. atractyloside found in the roots and seeds. It was thought worthwhile to carry out the hepatotoxic assessments and safety and toxicity evaluations of oral administration of atractyloside and methanolic extracts of *X. strumarium* L. in Albino Wistar rats. So, present investigation was undertaken with following objectives: To develop standardized protocols for Extraction, isolation, purification, characterization and quantitative estimation of Atractyloside; Hepatotoxic assessments of oral administration of atractyloside in Albino Wistar rats and; To study the safety and toxicity evaluation of methanolic extract in Albino Wistar rats. *Xanthium strumarium* Linn. root and seeds were found to contain alkaloids, anthraquinones, flavonoids, atractyloside, phenolics, steroids, terpenoids, and resin etc. In the present investigation, attempt was made to separate the atractyloside by using instant preparative thin layer chromatography (IPTLC) technique. Purified atractyloside was chemically characterized by IR, Mass and NMR spectral analysis. Atractyloside concentrations were found to be 2.9 and 4.3 mg/ml in plant root and seeds respectively using HPLC techniques. During hepatotoxic assessment, atractyloside produced severe hepatotoxicity in Albino Wistar rats. Observations of the sub-acute and acute toxicity studies had indicated that methanolic extract of *X. strumarium* had shown a narrow safety margin in animals. On the basis of sub-acute and acute toxicity evaluation studies, it was established that both atractyloside and methanolic extract of *X. strumarium* L. possess a narrow safety margin in rats used in in-vivo experimental and preclinical pharmacological studies.

Speaker Biography

Bhanu P S Sagar had completed his PhD from Jamia Hamdard, Post-doc from National Institute of Immunology and DSc in Alternative Medicine. He is presently the Director of Pharmacy College at IEC-GI & Former Vice-Chancellor of IEC University and has published 47 papers and presented 30 papers. He has presented two papers in "AAPS 2006 National Biotechnology Conference" in Boston, USA. He is evaluator for various international journals and also selected for "Marquis Who's Who in Asia" and "Marquis Who's Who in World". He has received many awards and prime areas of research include Plant Tissue Culture, Phytochemical & Pharmacological investigations of natural products.

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Neuropotential role of Taurine: Role of neurotransmitters, oxidative stress, mitochondrial dysfunctioning and histopathological evidences

Manveen Bhardwaj and **Anil Kumar**
Panjab University, India

Rationale: Alterations in neurotransmitters levels is the main culprit of the epilepsy. With the antioxidant effects, taurine cause the alterations in the Glutamate and GABA levels. But its mechanism of action in epilepsy is still undeciphered. Thus, there exists rationale in preventing the glutamate excitotoxicity by taurine as neuroprotective strategy in pentylenetetrazole (PTZ) induced kindling epilepsy.

Objective: Aim of present study is to investigate the neuroprotective role of taurine and its modulation by minocycline (Mino) in the kindling epilepsy.

Method: PTZ (40 mg/kg, i.p.) was administered alternatively for 29 days until animal exhibited full motor seizures. Taurine was given orally at a dose of 25, 50 and 100 mg/kg by dissolving it in distilled water once a day 1 h prior to PTZ treatment and minocycline at the dose of 50 and 100 mg/kg and its combination (Taurine 50 mg/kg + Mino50 mg/kg) and (Taurine 100 mg/kg + Mino100 mg/kg) for the period of 29 days. Various neurobehavioral parameters followed by biochemical, mitochondrial respiratory enzyme complexes (I-IV), neurotransmitter examinations (Glutamate, GABA, Serotonin, Dopamine and Norepinephrine) by HPLC and histopathological alterations by haematoxylin and eosin stain were assessed.

Results: PTZ administration significantly impaired the cognitive performance in the morris water maze (MWM) performance test, increased the seizure score, caused oxidative stress, mitochondrial dysfunctioning and also caused alterations in the neurotransmitter levels and in the histopathology of hippocampus and cortex. Treatment with the taurine (25, 50 and 100 mg/kg), minocycline (50 and 100 mg/kg) for 29 days significantly improved the seizure score, reduced AChE activity, oxidative damage (reduced LPO, nitrite level and elevate the SOD, catalase and GSH levels) and also restored the mitochondrial complexes (Complex I, II and IV) and improved the neurotransmitter levels (Glutamate, GABA, Serotonin, Dopamine and Norepinephrine). Combination of taurine with minocycline showed more significant effects as compared to the per se effect. Further, histopathological alterations showed the significant improvement effects in the combination of taurine with minocycline.

Conclusion: Taurine when combined with minocycline show the neuroprotection by decreasing the glutamate excitotoxicity against the PTZ induced kindling epilepsy.

Speaker Biography

Manveen Bhardwaj is a PhD Research Scholar at Panjab University, Chandigarh, India. She did her M. Pharmacy I.S.F college of Pharmacy, Moga in the year 2013. She has been awarded with "Young Scientist Award" at Punjab science congress at SUS college of Tangori Mohali.

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