



20th World Congress on
**TOXICOLOGY AND
PHARMACOLOGY**

May 06-07, 2019 Tokyo, Japan

Scientific Tracks & Abstracts
Day 1

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Pharmacological optimization of the conditioning regimen for hematopoietic stem cell transplantation

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Hematopoietic stem cell transplantation is an effective treatment for a variety of hematological disorders. Its success partly depends on the optimization of the pre-transplant conditioning regimen. To identify an efficacious regimen, we exposed cells to different drug combinations, analyzed their cytotoxicity and identified their molecular mechanisms of interaction using various techniques. We have shown the synergistic cytotoxicity of DNA Alkylating Agents (AA) and Nucleoside Analogs (NA) in leukemia and lymphoma cells and proposed a mechanistic model called the loop of death. Exposure of cells to a nucleoside analog initiates DNA damage resulting in chromatin remodeling and makes genomic DNA more susceptible to DNA alkylation. DNA damage response is then activated and the loop of DNA damage, chromatin remodeling and DNA alkylation continues until the tumor cells commit to apoptosis. Using this model and the [AA+NA] combination as a backbone to identify drugs that may further enhance its anti-tumor activity, we hypothesized that epigenetic modifiers would amplify the loop of death. Indeed, inhibitors of Histone Deacetylases (HDACi) and DNA Methyl Transferases (DNMTi), which facilitate relaxation of chromatin, were found to be synergistic with [AA+NA]. Since active DNA repair may contribute to decreased efficacy of these drug combinations, we also examined the inclusion of DNA repair inhibitors such as olaparib. Addition of olaparib to [AA+NA] caused significant apoptosis by activation of the DNA, damage response, inhibition of PARP activity and DNA repair, production of reactive oxygen species and depolarization of the mitochondrial membranes. Overall, our pre-clinical and clinical results suggest that the conditioning regimen for HSCT may be optimized by combining drugs that provide synergistic cytotoxicity based on their molecular mechanisms of action.

Biography

Ben C Valdez has completed his PhD in Biochemistry at Louisiana State University. He has completed his Post-doctoral training at Baylor College of Medicine in Houston, Texas. His current research focuses on the identification of safe and efficacious conditioning regimen for hematopoietic stem cell transplantation for patients with hematological disorders.

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Differences between cytotoxicity of preservatives used in cosmetic industry determined on consecutive passages of senescent diploid human lung fibroblasts *in vitro***Katarzyna Miranowicz-Dzierżawska, Lidia Zapor, Jolanta Skowroń and Lilianna Marciniak**
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Introduction & Aim: Cell culture system could be a useful model for aging-related changes. The aim of the study was to assess whether there are differences between the results of determination of preservatives cytotoxicity obtained on senescent cells in different age.

Method: Experiments were conducted to determine the cytotoxicity of four preservatives: Methylparaben, propylparaben, 2-phenoxyethanol and benzalkonium chloride on subsequent passages of senescent human lung CCD-8Lu (ATCC[®] CCL-201[™]) fibroblasts. The tests were carried out in passages no. 10/18. Xenobiotics cytotoxicity was evaluated using two cell viability assays: MTT assay, determining metabolic activity of cells and NRU assay, assessing the integrity of cell membranes. The IC₅₀ values were used as the main measure for comparing the cytotoxicity of tested compounds.

Results: The results showed that the preservatives can be ranked according to the increasing cytotoxic potency towards the tested human diploid lung fibroblasts: 2-phenoxyethanol < methylparaben < propylparaben < benzalkonium chloride. Older cells became less susceptible than the younger ones with cytotoxic effects of the xenobiotics tested in the majority of cases.

Conclusion: The passage number of diploid human lung fibroblasts had an important impact on the susceptibility of cells to preservatives. The test of the integrity of cell membranes (NRU) seems to be more appropriate to assess the cytotoxic effect of the investigated preservatives on diploid fibroblasts in different ages, which may be related to the mechanism of action of these compounds.

Biography

Katarzyna Miranowicz-Dzierżawska is currently working in Laboratory of Toxicology, a part of the Department of Chemical, Aerosol and Biological Hazards in the Central Institute for Labour Protection, National Research Institute. She has completed her graduation from Faculty of Pharmacy with Pharmaceutical Analysis specialization of the Medical University of Warsaw and PhD from Jagiellonian University, Cracow.

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Scientific Tracks & Abstracts
Day 2

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Studies on the assessment of pesticide induced stress and apoptosis in fresh water teleost *Channa punctatus*

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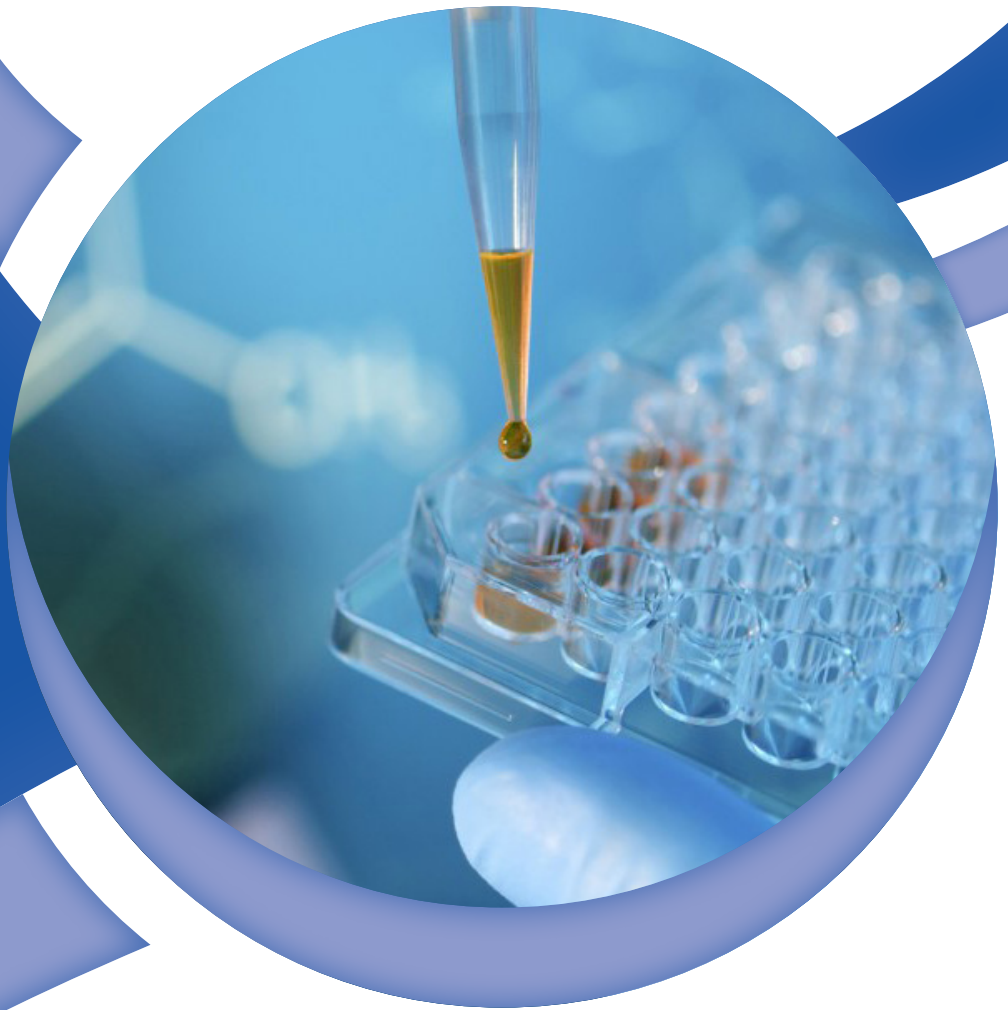
The application of chemical pesticides to agricultural land very often contaminate aquatic habitat which in turn causes detrimental effects to the aquatic biota particularly to the economically important non-target organisms like fish. The aim of the present study was to explore the impact of pesticides (triazophos, deltamethrin and their combination) on oxidative stress level in fish, *Channa punctatus*. The fishes were procured from local animal supplier of Allahabad, India and acclimatized in laboratory condition. The fishes were exposed to different concentrations of pesticides for 96 hours. The LC₅₀ (Lethal Concentration) value for triazophos, deltamethrin and their combination were found to be 0.069 mg/l, 7.17 µg/l and 0.032 mg/l respectively. For the sub-lethal study, fishes were exposed to 5% and 10% of LC₅₀ of pesticides for 96 hours. During the exposure period, the behavioral changes (i.e. opercular movement, surfacing) were observed. Immediately after exposure, the animals were sacrificed and blood and the key organs (brain, liver, kidney, gills and muscles) were collected for biochemical/stress enzymes assay and for apoptotic studies. In the blood parameters, TLC and DLC showed significant change in counts as compared to control with increased rate of apoptosis. In the stress related enzyme activity such as SOD, CAT, GST and levels of GSH and LPO (Lipid Peroxidation) significant changes were recorded with increase in concentration of pesticides. From our study conclude that, the dose dependent exposure of pesticides may impose detrimental threat to the fish population.

Biography

Shikha Singh is currently working as a Doctoral Fellow at University of Allahabad, India. She has completed her Masters of Science with cytogenetic specialization from University of Allahabad, India. She has presented ten oral posters in different international/national conferences organized in India. She has been awarded with Best Oral Presentation award for her work in Indian Science Congress Association. She also assists as resource person in various academic courses.

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Video Presentations
Day 2

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Hepatoprotective effects of omega-3 fatty acids through the modulation of genes involved in lipid metabolism and inflammatory pathway in alcohol induced hepatotoxicity

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Omega-3 fatty acids offer several health benefits. In present investigation, hepatoprotective potential of omega-3 fatty acids in the form of flax oil and fish oil was assessed against repeated alcohol dosing in male albino Wistar rats. Hepatic injury was induced by administering 30 % alcohol (1ml/100g b.w./day, p.o). Flax oil and fish oil (500mg/kg b.w./day, p.o) were administered to hepatotoxicity induced rats. Biochemical parameters were analyzed from serum and liver tissue. The expressions of fatty acid binding protein 1 (FABP1), peroxisome proliferator activated receptor gamma (PPAR γ), sterol regulatory element binding protein 1 (SREBP1), nuclear factor kappa β (NF- κ β) and tumor necrosis factor alpha (TNF- α) genes from liver were assayed by semi-quantitative polymerase chain reaction. Administration of flax oil or fish oil prevented hepatic damage with marked improvement in hepatic function and normalization of lipid profiles in serum and liver. These interventions normalized oxidative stress through improvements in levels of anti-oxidant enzymes and oxidative stress markers. Expression of genes such as FABP1, PPAR γ were downregulated and SREBP1, NF- κ β and TNF- α were upregulated in alcohol induced hepatotoxic rats while treatment with flax oil and fish oil showed improvement in these gene expression. Histological analysis showed normal hepatic architecture in flax oil and fish oil treated animals. The flax oil was found could protect the liver against alcohol-induced liver toxicity and oxidative stress. However, further clinical studies are required to assess the safety and benefits of flax oil in human beings.

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Toxicological evaluation of chlorpyrifos, cypermethrin and their combination in earthworm and their impact on acetylcholinesterase

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The increasing applications of pesticides in the agricultural fields have adverse impact on flora and fauna of the soil ecosystem. The role of earthworms in the agricultural practices is well known as they immensely contribute in increasing the quality and fertility of soil. So, it acts as a bio-indicator for the ecotoxicological analysis of pesticide induced soil pollution. Therefore, the present study was aimed to explore the impact of chlorpyrifos (an organophosphate; OP), cypermethrin (a pyrethroid) and their combination (chlorpyrifos+cypermethrin) on earthworm, *Eudrilus eugeniae*. *E. eugeniae* were exposed to different concentrations of pesticides for 48 hours by paper contact toxicity method. The LC₅₀ for commercial grade chlorpyrifos, cypermethrin and their combination were determined as 0.165, 0.020 and 0.066 µg/cm² respectively. To assess the sub-lethal effect of these pesticides, *E. eugeniae* were exposed to 5% and 10% of LC₅₀ pesticides for 48 hours. Alterations in morpho-behavioral patterns such as coiling, clitellar swelling, mucus release and bleeding followed by fragmentation of body in earthworms were observed following exposure. Acetylcholinesterase (AChE) activity was assayed in different regions of body segment which exhibits significant ($p < 0.05$) decrease in AChE activity particularly in pre-clitellar region followed by clitellar and post-clitellar regions and in comparison, to whole body. The decreased AChE activity with increasing concentration of pesticides indicates the effect at neuronal level which apparent from the behavioral changes. Therefore, from the present findings it can be concluded that long term exposure to these pesticides could lead to severe and irreparable effects on biochemical mechanisms of earthworms.

Biography

Rishikesh Kumar Tiwari is presently working as a Doctoral Fellow with Professor Ravi S Pandey, Biochemistry Laboratory, Department of Zoology, University of Allahabad. He has completed his MSc with Cytogenetics specialization from University of Allahabad, India. He has 10 research/review articles in national/international journal of repute and one book chapter in USA based publishing house.

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