PROGRAMME AND ABSTRACT BOOK

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WELCOME MESSAGE FROM THE CHAIR OF MYCOT 2022

Dear Distinguish speakers and friends,

It is a pleasure for me to welcome you to MyCOT 2022.

The theme of MyCOT 2020 is Advances in Toxicology Post Covid-19 Disruption: Risk Assessment & Public health management. Therefore, an attractive activities of 2 days has been set up with an aim to facilitate collaboration in education and research in the field of toxicology. It is hoped that during the Congress, fruitful interactions among participants and new proposals can grow up for the intellectual growth of all the participants.

On behalf of the Organizing Committee, I would like to express my appreciation to all the scientist who share their valuable research on the latest advancement and challenges in the field of toxicology with the participants of this congress. Thank you for contributing to high quality paper in the Supplementary issue of the Malaysian Journal of Medicine and Health Sciences-MyCOT 2022.

My special thanks to the dedicated organizing committee that has made this congress happen despite various post COVID-19 pandemic challenges.

I wish you all enjoyable and productive congress.

Assoc. Prof. Dr. Razinah Sharif
Chair of the MyCOT 2022

MYSOT PRESIDENT MESSAGE

Dear Distinguish speakers and friends

It is my pleasure to welcome you to the 4th Malaysian Congress of Toxicology (MyCOT 2022). This is our first physical meeting since COVID 19 hit us back in 2020. The theme of MyCOT 2020 is Advances in Toxicology Post Covid-19 Disruption: Risk Assessment & Public health management' is timely with our post COVID-19 situation.

Malaysian Society of Toxicology (MySOT) has been providing programmes and activities consistence with the environmental and health concerns of our communities. This congress shall provide an opportunity for the presentation of updated results related to toxicology research. Most importantly bringing together scientists from academic institutions and industry thus promoting professional interactions between them. Furthermore, the meeting has also included a one-day workshop entitled 'Zebrafish Embryos as an *In Vivo* Toxicity Model'.

I would like to congratulate dedicated organizing committee to make this congress happen despite various challenges post COVID-19 pandemic.

I wish you all a great meeting and a productive interaction with colleagues in this congress.

Your sincerely

Dr Rozaini Abdullah

President,
Malaysian Society of Toxicology (MySOT)

PROGRAMME:

WORKSHOP IN-CONJUNCTION WITH THE MyCOT 2022

15th NOVEMBER 2022 (TUESDAY)
Zebrafish Embryos as an *In Vivo* Toxicity Model Workshop at Central Research & Animal Facility (CREAM), IIUM, Kuantan

MyCOT 2022 - DETAILED SCHEDULE

Main Venue
Kulliyah of Nursing, IIUM, Kuantan

DAY 1: 16th NOVEMBER 2022 (WEDNESDAY)

REGISTRATION & OPENING CEREMONY

HALL 1 – AUDITORIUM, LEVEL 1	
Time	Title
08.00 am - 08.30 am	Registration
Emcee: Dr. Mohd Hanif Jainlabdin (International Islamic University Malaysia)	
08.30 am - 08.35 am	Doa recital
08.35 am - 08.40 am	National anthem
08.40 am - 08.45 am	**Welcoming remarks** Associate Professor Dr. Razinah Sharif *(Chairman of Malaysian Congress of Toxicology 2022)*
08.45 am - 09.00 am	**Opening ceremony** Profesor Emeritus Tan Sri Dato' Dzulkifli bin Abdul Razak *(Rector of International Islamic University Malaysia)*

KEYNOTE LECTURE

HALL 1 – AUDITORIUM, LEVEL 1	
Chairperson: Dr. Rozaini Abdullah (Universiti Putra Malaysia)	
Time	Title
09.00 am – 10.00 am	**Management of chemicals through product stewardship** Dr. Salmaan Hussain Bin Inayat Hussain *(Petroliam Nasional Berhad, Malaysia)*
10.00 am – 11.00 am	*Tea break (Exhibition Area, Level 1)* ***Poster session 1 (Resource Centre, Level 1)***

PARALLEL SESSIONS

HALL 1 – AUDITORIUM, LEVEL 1	
REGULATORY TOXICOLOGY	
Chairperson: Professor Dr. Suzanah Abdul Rahman (International Islamic University Malaysia)	
Time	Title

11.00 am – 11.30 am	**Hazard communication throughout the product life cycle in Malaysia from the perspective of regulatory toxicology** Dr. Jahangir Kamaldin *(AMDI USM, Malaysia)*
11.30 am – 12.00 pm	**Regulatory pre-clinical toxicology requirement for vaccine development** Dr. Hussin Muhammad *(Institute for Medical Research, Malaysia)*
12.00 pm – 12.30 pm	**OECD QSAR toolbox screening of toxicity endpoints of chemicals in research and development (R&D)** Dr. Sara Shahruddin *(Petronas Research Sdn. Bhd., Malaysia)*
12.30 pm - 2.00 pm	*Lunch break (Exhibition Area – Level 1)*
MEDICAL TOXICOLOGY	
Chairperson: Dr. Shafinaz Abd Gani (Universiti Putra Malaysia)	
02.00 pm – 02.30 pm	**A multiagency and proactive approach to reduce drug-related harm in New South Wales, Australia** Dr. Thanjira Jiranantakan *(Centre for Alcohol and Other Drugs, NSW Ministry of Health, Australia.)*
02.30 pm – 03.00 pm	**Aristolochic acid-associated nephrotoxicity and cancers in Europe: Implications for a preventable global public health risk** Dr. Jiri Zavadil *(International Agency for Research on Cancer, France)*

HALL 2 - MULTIPURPOSE HALL, LEVEL 2	
NATURAL PRODUCTS TOXICOLOGY	
Chairperson: Dr. Salfarina Ramli (Universiti Teknologi MARA)	
Time	Title
11.00 am – 11.30 am	**Plant-based immunomodulators with antitumor activity: An insight on their mechanisms of action** Dato Professor Dr. Ibrahim Jantan *(Universiti Kebangsaan Malaysia, Malaysia)*
11.30 am – 12.00 pm	**HPLC fingerprint a powerful tool for quality control of herbal products** Dr. Athip Sakunphueak *(Prince of Songkla University, Thailand)*
12.00 pm – 12.30 pm	**Assessing the toxicity of sibutramine chloride-adulterated weight loss supplements in rats** Dr. Suparmi *(Universitas Islam Sultan Agung, Indonesia)*
12.30 pm - 2.00 pm	*Lunch break (Exhibition Area – Level 1)*
ENVIRONMENTAL TOXICOLOGY	
Chairperson: Dr. Nazzatush Shimar Jamaludin (Universiti Malaya)	
02.00 pm – 02.30 pm	**Polycyclic aromatic hydrocarbon in Kuala Lumpur urban environment and its effect on human health** Professor Dr. Mohd Talib Latif *(Universiti Kebangsaan Malaysia, Malaysia)*
02.30 pm – 03.00 pm	**Regulatory toxicology vs occupational toxicology at the workplace** Mrs. Hazlina Yon *(DOSH, MOHR)*
03.00 pm – 03.30 pm	**Genotoxic interactions of environmental pollutants, malnutrition and SARS-Cov-2 virus may exacerbate the COVID-19 pandemic** Professor Dr. Michael Fenech *(University of South Australia, Australia)*

TOXICOLOGY RESEARCH SHARING

HALL 1 - AUDITORIUM, LEVEL 1 (PHYSICAL PRESENTATION)	
Chairperson: Assistant Professor Dr. Noor Fatihah Mohamad Fandi (International Islamic University Malaysia)	
Time	Title
03.30 pm – 03.40 pm	**Detection of mycotoxins in old buildings: Occupational exposure and health risk assessment** Mrs. Anis Syuhada Omar Hamdan *(Universiti Sains Malaysia)*
03.40 pm – 03.50 pm	**Synthesis of phosphanecopper(I) benzoylthiourea complexes and their acute toxicity studies in embryo of zebrafish** Ms. Nur Zulaikha Izzati binti Rosman *(Universiti Malaya)*
03.50 pm – 04.00 pm	**Exposure to dioxins from peatland fires induces oxidative DNA among firefighters in Malaysia** Mr. Ahmad Shalihin Bin Mohd Samin *(National Poison Centre, Universiti Sains Malaysia, Malaysia)*
04.00 pm – 04.10 pm	**Polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/FS) occurrence and profiles in Malaysian peat** Ms. Khairulmazidah Mohamed *(Universiti Sains Malaysia)*
04.10 pm – 04.20 pm	**NMR-metabolomics: Therapeutic potential of fermented soybean extract against lead (Pb) toxicity using zebrafish model** Ms. Chong Siok Geok *(Universiti Putra Malaysia)*
04.20 pm – 04.30 pm	**Toxicity of *Piper sarmentosum* leaf extract in different solvent systems against zebrafish (*Danio rerio*) embryos** Dr. Suhaili Shamsi *(Universiti Putra Malaysia)*
04.30 pm – 04.40 pm	**Streptozotocin toxicity in mice retinal layer function** Ms. Yamunna Paramaswaran *(AIMST University)*
04.40 pm – 04.50 pm	**Presence of pyrrolizidine alkaloids in registered natural products in Malaysia** Mrs. Nur Azra Binti Mohamad Pauzi *(Universiti Putra Malaysia)*
04.50 pm – 05.00 pm	**Procyanidin-c1 alleviates bisphenol AF-induced apoptosis, oxidative stress and mitochondrial damage in the early developmental stages of zebrafish embryos** Mr. Razif Dasiman *(Universiti Teknologi MARA, Malaysia)*
05.00 pm	*Tea break (Exhibition Area – Level 1)* ***End of Day 1***

HALL 2 - MULTIPURPOSE HALL, LEVEL 2 (VIRTUAL PRESENTATION)	
Chairperson: Dr. Zulkhairul Naim bin Sidek Ahmad (Universiti Malaysia Sabah)	
Time	Title
03.30 pm – 03.40 pm	**Heavy metals in bauxite: A summary of toxicological implications on communities in Bukit Goh, Kuantan** Professor Dr. Zailina Hashim *(Universiti Putra Malaysia)*
03.40 pm – 03.50 pm	**Pesticide usage and cholinesterase enzyme inhibition in farmers of selected sites of Bhutan** Mr. Adeep Monger *(Royal Center for Disease Control, Bhutan)*
03.50 pm – 04.00 pm	**The molecular mechanism of triphenyltin(IV) diisopropyldithiocarbamate-induces cytotoxicity in K562 human erythroleukaemia cells** Ms. Sharifah Nadhira Binti Syed Annuar *(Universiti Kebangsaan Malaysia)*
04.00 pm – 04.10 pm	**The toxicity of streptozotocin on the micro-anatomical changes of the retina in diabetic mice** Dr. Aswinprakash Subramanian *(AIMST University)*
04.10 pm – 04.20 pm	**Assessment of wound healing potential using *Eleusine indica* leaves extract on Sprague Dawley rats** Ms. Nur Hidayati Binti Osman *(Universiti Kebangsaan Malaysia)*
04.20 pm – 04.30 pm	**Pathophysiological perspective of aluminium chloride-induced neurovascular toxicity in rats** Mr. Sohrab A. Shaikh *(AIMST University)*
04.30 pm – 04.40 pm	**Potential toxic effects of streptozotocin on vascular system in rats** Mr. Lim Khian Giap *(AIMST University)*
04.40 pm – 04.50 pm	**Effects of 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) on RWPE-1 cell line** Dr. Siti Nazmin Saifuddin *(AMDI USM, Malaysia)*
04.50 pm	*Tea break (Exhibition Area – Level 1)* ***End of Day 1***

DAY 2: 17th NOVEMBER 2022 (THURSDAY)

KEYNOTE LECTURE

HALL 1 – AUDITORIUM, LEVEL 1	
Chairperson: Associate Professor Dr. Razinah Sharif (Universiti Kebangsaan Malaysia)	
Time	Title
09.00 am – 10.00 am	**Chemical risk assessment: Changes and challenges** Dr. Richard Brown *(World Health Organization)*
10.00 am - 10.30 am	*Tea break (Exhibition Area – Level 1)*

PARALLEL SESSIONS

HALL 1 – AUDITORIUM, LEVEL 1	
ADVANCES IN TOXICOLOGY	
Chairperson: Dr. Mary Khoo Gaik Hong (Forest Research Institute Malaysia)	
Time	Title
10.30 am – 11.00 am	**Role of endogenous cyanide in the detoxification of selenium** Professor Dr. Yasumitsu Ogra *(Chiba University, Japan)*
11.00 am – 11.30 am	**Essential role of computational toxicology in optimizing drug discovery** Associate Professor Dr. Vannajan Sanghiran Lee *(Universiti Malaya, Malaysia)*
11.30 am – 12.00 pm	**Dioxins emission prediction from peat soil using artificial neural networks (ANN)** Dr. Leong Yin Hui *(National Poison Centre, Universiti Sains Malaysia, Malaysia)*
12.00 pm – 01.00 pm	**Poster session 2 (Resource Centre – Level 1)**
01.00 pm - 02.30 pm	*Lunch break (Exhibition Area – Level 1)*
REGIONAL ISSUES IN TOXICOLOGY	
Chairperson: Associate Professor Dr. Syahida Ahmad (Universiti Putra Malaysia)	
02.30 pm – 02.55 pm	**Impacts of developmental exposure to PFAS on human health: The Hokkaido birth cohort study** Professor Dr. Reiko Kishi *(Hokkaido University, Japan)*
02.55 pm – 03.20 pm	**Safety of herbal medicine: The Southeast Asia scenario** Dr. Ami Fazlin Syed Mohamed *(Institute for Medical Research, Malaysia)*
03.20 pm – 03.45 pm	**Clinical toxinology and its development and progress in Malaysia** Dr. Ruth Sabrina Safferi *(President of Malaysian Society of Toxinology)*
03.45 pm - 04.10 pm	**Diet, genomic stability and relative cancer risk: Where Malaysia stands?** Associate Professor Dr. Razinah Sharif *(Universiti Kebangsaan Malaysia)*

HALL 2 - MULTIPURPOSE HALL, LEVEL 2	
NANOTOXICOLOGY	
Chairperson: Dr. MD Abul Kalam Azad (MAHSA University)	
Time	Title
10.30 am – 11.00 am	**Amorphous silica exposure in the development of chronic kidney disease of unknown etiology within agricultural workers** Professor Dr. Jared Brown *(Colorado Center for Nanomedicine and Nanosafety, USA)*
11.00 am – 11.30 am	**Toxicity evaluation of inhaled iron oxide nanoparticles with different surface charge polarities against pulmonary cells** Dr. Lee Wing Hin

	(Universiti Kuala Lumpur, Malaysia)
11.30 am – 12.00 pm	**Proteomics analysis to compare the toxicological pathways of silver nanoparticle in skin carcinoma cell and zebrafish embryo** Dr. Pawitrabhorn Samutrtai *(Chiang Mai University, Thailand)*
12.00 pm – 01.00 pm	**Poster session 2 (Resource Centre – Level 1)**
01.00 pm - 02.30 pm	*Lunch break (Exhibition Area – Level 1)*
DEVELOPMENTAL & REPRODUCTIVE TOXICOLOGY	
Chairperson: Dr. Redzuan Nul Hakim Abdul Razak (International Islamic University Malaysia)	
02.30 pm – 03.00 pm	**New approach methods (NAMs) on reproductive toxicology from petroleum substances** Dr. Lenny Kamelia Zhuo *(Shell, Netherlands)*
03.00 pm – 03.30 pm	**Environmental toxicants and metabolic disorders: impact on reproductive health concerns** Dr. Giribabu Nelli *(Universiti Malaya, Malaysia)*

AWARDS & CLOSING CEREMONY

HALL 1 – AUDITORIUM, LEVEL 1	
Emcee: Dr. Salfarina Ramli (Universiti Teknologi MARA) & Dr. Nurul Farahana Kamaludin (Universiti Kebangsaan Malaysia)	
Time	Title
04.15 pm - 05.00 pm	**Awards Presentation** **Closing ceremony** Dr. Rozaini Abdullah *(President of Malaysian Society of Toxicology)*
05.00 pm	*Tea break / Networking session (Exhibition Area – Level 1)* ***End of MyCOT 2022***

LIST OF KEYNOTE & INVITED SPEAKERS/ORAL PRESENTERS

[KEY-1]

MANAGEMENT OF CHEMICALS THROUGH PRODUCT STEWARDSHIP

Salmaan H Inayat-Hussain

Head, Environment, Social Performance & Product Stewardship, Group Health, Safety & Environment, Petroliam Nasional Berhad, Level 13, Tower 1, PETRONAS Twin Towers, Kuala Lumpur, Malaysia

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ABSTRACT

Product stewardship is key in managing chemical safety through a sound management of chemicals throughout their lifecycle to ensure that chemicals are produced and used in ways that minimize significant adverse impacts on human health and environment. This is aligned with the UN Sustainable Development Goals, the world's comprehensive plan of action, which includes goals to ensure good health and well-being and responsible consumption and production. In order to achieve these goals, industries need to integrate product stewardship to protect workers and community members against adverse health outcomes from chemical exposure. This talk will discuss the current approaches and examples of product stewardship and regulatory toxicology implementation especially from the energy industry.

KEYWORDS: Product stewardship; regulatory toxicology; sustainable development goals; chemicals

[KEY-2]

CHEMICAL RISK ASSESSMENT: CHANGES AND CHALLENGES

Richard Brown

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ABSTRACT

Chemical risk assessment plays a key role in managing chemicals to protect public health. In the areas of toxicological mechanisms, in new testing methods and other disciplines like biomonitoring, the science underpinning risk assessment is developing rapidly. At the same time, the demands on the risk assessment process from risk managers and from wider society are increasing, for greater understanding of how risk assessments were undertaken and the uncertainties around conclusions. Decision-making for the use of chemicals also has to operate within a framework of wider concerns - such as demands for greater sustainability and mitigating the effects of climate change. This takes place against a background where the burden of disease from exposure to chemicals is already substantial and is increasing, and where the production and use of chemicals is set to increase significantly over the coming years. This talk will describe some of the ways that the practise of toxicology and risk assessment has changed over the past 20 years, from experimental methods to new risk assessment frameworks. The progress which has been made to address some of the gaps - such as incorporating problem formulation, systematic approaches, methods for assessing combined exposures and characterising uncertainties - will be highlighted. Many challenges remain - increasing complexity, inadequate surveillance, misinformation and challenges to the credibility of the chemical risk assessment process. This talk will provide an overview of these issues and challenges, drawn from a global context and with reference to where the WHO can play a role.

[INV-1]

HAZARD COMMUNICATION THROUGHOUT THE PRODUCT LIFE CYCLE IN MALAYSIA FROM THE PERSPECTIVE OF REGULATORY TOXICOLOGY

Jahangir Kamaldin[1*], Nur Nadhirah Mohamad Zain[1] and Maisarah Nasution Waras[1]

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ABSTRACT

Introduction: The expression of the phrase Cradle to Grave or Womb to Tomb reflects the chemical substance life cycle from the initial synthesis that begins at the R&D stage and eventually ends as waste being disposed. The likelihood of the chemical substance being exposed to humans and the environment covers both ends of the life cycle. The presentation aims to discuss whether the existing legislation in Malaysia had addressed the hazard communication particularly the toxicity to the users of the chemical substance throughout its life cycle. The role of the regulatory bodies in enforcing the legislation is also discussed.

Method: Information on the published legislation in Malaysia up to June 2022 were gathered from the online search engine that was accessible to the public. The gathered materials were either in Bahasa Melayu or English and those published by the regulatory bodies were prioritized as authentic information.

Results: Malaysia has more than one law that addresses the chemical substance toxicity hazard communication at the different stages of the chemical substance life cycle. Furthermore, these laws are enforced by different regulatory bodies. The scope of some of the laws mainly covers the end-consumer product while some others focus on chemical substances utilised by industries.

Conclusion: Regulatory bodies in Malaysia regulates the chemical substance hazard communication within the defined scope of the legislation consistent with their establishment.

KEYWORDS: Toxicity; hazard communication; chemical life cycle; regulatory; legislation

[INV-2]

REGULATORY PRE-CLINICAL TOXICOLOGY REQUIREMENT FOR VACCINE DEVELOPMENT

Hussin Muhammad

Institute for Medical Research, Malaysia

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ABSTRACT

Coronavirus disease 2019 (COVID-19) has been the cause of millions of deaths and also social and economic crises worldwide. The scientific community from different public organizations and pharmaceutical industries has been exploring all strategies to develop and make available efficient vaccines against SARS-CoV-2 to the public, which is essential to protect and reduce severe illness and death. Development of a new vaccine involves many phases including exploratory, pre-clinical studies, clinical trials, regulatory authorization or approval, manufacturing, and marketing. Although COVID-19 vaccines were developed rapidly, all steps have been taken to ensure their safety and effectiveness. Vaccines typically produce various clinical effects due to the activation of various components of the immune system like proinflammatory cytokines which contributes to the systemic toxicity. Therefore, a proper study design for the pre-clinical safety assessment which consists of general and specific toxicology studies is required for the regulatory and registration purposes.

KEYWORDS: Vaccine; pre-clinical; regulatory; COVID-19; registration

[INV-3]

ARISTOLOCHIC ACID-ASSOCIATED NEPHROTOXICITY AND CANCERS IN EUROPE: IMPLICATIONS FOR A PREVENTABLE GLOBAL PUBLIC HEALTH RISK

Jiri Zavadil

International Agency for Cancer Research (IARC/WHO), Lyon, France

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ABSTRACT

Aristolochic acid (AA), a powerful nephrotoxin and mutagenic carcinogen (IARC Group 1), is present in essentially all species of the *Aristolochiacae* plant family. Exposure to AA can elicit serious nephrotoxic effects (aristolochic acid-associated nephropathy, AAN), and is a significant risk factor for urologic, hepatobiliary and possibly other cancer types due to specific damage of the DNA in the target tissues. Major breakthroughs in our understanding of the causes and the clinico-pathological features of AAN and AA-associated cancers had been achieved by multidisciplinary research of two major AAN occurrences in Europe. One setting involves endemic nephropathy in particular farming areas of Southeastern Europe and represents an example of chronic, environmental exposure to AA due to dietary contamination. The other, recorded in Belgium in the 1990's, illustrates an AAN outbreak due to alternative medical treatment and unsatisfactory regulation of traditional herbal medicines.

Molecular analyses performed in these two well-studied settings will be presented, including genome-wide screens for a specific somatic mutational signature of AA and its use for tracking of the origins of various cancer types as well as of multiple tumours arising in AAN patients. Despite the available research evidence for AA carcinogenicity and nephrotoxicity, *Aristolochia* herbs continue to be marketed worldwide as traditional herbal medicinal products, while possible environmental exposure routes receive inadequate attention. The implications for future studies in exposed at-risk populations will be discussed, alongside the potential avenues for worldwide prevention of AAN and AA-associated cancers.

[INV-4]
A MULTIAGENCY AND PROACTIVE APPROACH TO REDUCE DRUG-RELATED HARM IN NEW SOUTH WALES, AUSTRALIA

Thanjira Jiranantakan[1,2,3]

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[2]NSW Poisons Information Centre, Sydney Children's Hospitals Network, Westmead, Australia
[3]Edith Collins Centre, Central Clinical School, Faculty of Medicine and Health, The University of Sydney, Australia.

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ABSTRACT

Introduction: Illicit drug use results in adverse health, social and economic consequences for the user, their families and the wider community. A strategic approach and partnership among relevant agencies are essential to reduce drug harm.

Methods: This report aims to demonstrate the proactive approach to detect, respond, report and reduce drug-related harm coordinated by the Centre for Alcohol and Other Drugs, New South Wales (NSW) Ministry of Health.

Results: NSW Ministry of Health has worked closely with NSW Poisons Information Centre, hospital clinical toxicology services, NSW Health Pathology Forensic & Analytical Science Service, NSW Police Force, relevant agencies and community groups to detect illicit drugs circulated in NSW and to facilitate clinical management and public health responses. Detections of illicit substances include testing clinical samples through the Prescription, Recreational and Illicit Substances Evaluation (PRISE) Program (established in 2018); seized samples through the Combined Surveillance and Monitoring of Seized Substances (CoSMoSS) Project (established in 2019); and post-mortem toxicology results through monthly surveillance. Toxicology results reveal common and emerging substances such as 25C-NBOMe, ADB-BUTINACA, 2-FDCK, metonitazene, acetylfentanyl, methylone and flubromazolam. The NSW expert panel was established with members from multiple specialists and community representatives to perform a risk assessment and public health interventions. This presentation will include case studies to demonstrate the operations.

Conclusion: Toxicity surveillance and response in NSW has been operated successfully and has had multiple key detections with significant impacts on clinical management and public health interventions. It requires good collaboration between multiple agencies with central coordination.

KEYWORDS: illicit drug use; drug-related harm; toxicity surveillance; public health; multiagency approach

[INV-5]

PLANT-BASED IMMUNOMODULATORS WITH ANTITUMOR ACTIVITY: AN INSIGHT ON THEIR MECHANISMS OF ACTION

Ibrahim Jantan[1]

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ABSTRACT

There is a growing interest in the use of naturally occurring immunostimulants as supplements in combination with the common therapeutic modalities in treatment of cancer. Immunostimulants improve the immune response against tumors and reduce the suppressive effect produced by the chemotherapy along with the tumor itself to escape the immune surveillance. Plant-based immunostimulants can elicit and activate humoral and cell-mediated immune responses against tumor that facilitate the recognition and destruction of already existing tumor. Natural immunomodulators that induce the host immune cell activity can exhibit cytotoxic and antitumor effects through enhancement of phagocytic activity of immune cells, increased nitric oxide (NO) and reactive oxygen species (ROS) production and natural killer (NK) cells cytotoxic activity. Many natural products were reported to cause cell cycle arrest and anti-proliferative effect such as 6-gingerol, tangeritin , zerumbone and resveratrol. Natural immunomodulators are able to abolish the tumor propagation through disruption of tumor cell cycle and apoptosis induction. Whereas natural compounds with suppressive activity such as resveratrol, genistein, quercetin and curcumin can act as protective agents and prevent the initiation of tumor development mainly due to their antioxidant activity or free radical scavenger to prevent DNA damage and interfere with the uptake of toxic materials by the cells. The anticancer activity of these immunomodulators is due to their anti-inflammatory, antioxidant, and induction of apoptosis, anti-angiogenesis, and anti-metastasis effect. These natural immunomodulators can be used as prophylaxis against the initiation of cancer besides the inhibition of tumor growth and proliferation.

KEYWORDS: Natural immunomodulators, immunostimulants, immunosuppressants, apoptosis, anticancer

[INV-6]

HPLC FINGERPRINT A POWERFUL TOOL FOR QUALITY CONTROL OF HERBAL PRODUCTS

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ABSTRACT

Introduction: Herbal products contain hundreds of compounds and their quality depends on various factors such as geographical sources, harvest period and storage. Chromatographic fingerprint analysis has been suggested for assessing the quality of herbal medicines along with quantitative analysis of some important markers.

Methodology: In order to establish HPLC chromatographic fingerprint, 12 different sources of raw material or production lots were prepared. The HPLC conditions should be able to separate all the markers with satisfactory resolution. Linearity, precision, specificity and stability parameters were determined for validation. The fingerprints were obtained after all the data set has been analyzed for the similarity index, common peaks, characteristic peaks and strong peaks.

Results: In our works Chantaleela preparation, a Thai traditional medicine and *Mitragyna spciosa* leaf extract were investigated on their HPLC fingerprints and quantitative analysis. Chantaleela preparation showed a variety of the quality depending on raw material sources. The fingerprint of Chantaleela preparation was able to distinguish the preparation that used the wrong herbal component. The quality of *M. speciosa* was mainly dependent on raw material sources and raw material processing. It was found that mitragynine and some signal peaks disappeared during the inappropriate drying process.

Conclusion: The overall quality of herbal products can be determined by both quantitative analysis and qualitative analysis of fingerprints. HPLC fingerprints play a major role in the identification of the markers and other unknown compounds in the complex matrix while the quantitative analysis indicates product safety and efficacy.

KEYWORDS: HPLC fingerprint, herbal products, quality control, traditional medicine

[INV-7]
REGULATORY TOXICOLOGY VS OCCUPATIONAL TOXICOLOGY AT WORKPLACE

Ir. Ts. Hazlina Yon[1]

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ABSTRACT

Introduction: Hazardous chemicals are an ongoing concern and there are many cases of workers being severely affected by chemicals due to both acute and chronic exposure. Occupational toxicology is the application of the principles and methodology of toxicology to understanding and managing chemical and biological hazards encountered at work. Field of occupational toxicology is the study of the adverse effects of chemicals that may be encountered by workers during their employment. To investigate role of toxicology in Malaysia, an elaboration is given on existing legal requirements which made use of toxicological data, or the knowledge of health effects data in requirement of risk assessment and medical surveillance.

Role of toxicology: Risk assessment plays a very important role in chemical management where it provides better understanding of the impact of toxic chemicals on the exposed population. In Malaysia, the regulatory toxicology embedded in the Use and Standard of Exposure of Chemicals Hazardous to Health (USECHH) Regulations 2000 provides requirement of risk assessment, chemical exposure monitoring, biological monitoring and medical surveillance for those workers exposed to chemicals hazardous to health. Application of toxicological knowledge can be found in safety data sheets where it is also one of the duties of hazardous chemicals suppliers in Malaysia to prepare Safety Data Sheets for each hazardous chemicals supplied. Under the Classification, Labelling and Safety Sheets Regulation 2013, these data need to be supplied to enable classification for mixtures and to provide information to users of hazardous chemicals. There are exposure standards for 647 chemicals adopted from the American Conference of Governmental Industrial Hygienist (ACGIH) set for workplace exposure standards in the USECHH Regulations. Biological monitoring is an important tool to identify the nature and amount of chemical exposures in occupational and environmental situations. It involves the measurement of a chemical, its metabolite, or a biochemical effect in a biologic specimen for the purpose of assessing exposure.

Results: Risk assessment for those exposed to chemicals hazardous to health Malaysia using knowledge and information on toxicological data must be conducted according to the Manual of Recommended Practice on Assessment of the Health Risks arising from the Use of Chemicals Hazardous to Health at The Workplace 2018. Assessment is concluded based on the level of risk and the adequacy of existing control measures.

Conclusion: This paper elaborates the difference between occupational toxicology and regulatory toxicology. It also emphasizes the use of knowledge on toxicology in legal requirements in Malaysia to protect the workers from the deleterious effects of chemicals.

KEYWORDS: Regulatory toxicology, medical surveillance, biological monitoring, safety data sheets, USECHH Regulations

[INV-8]

POLYCYCLIC AROMATIC HYDROCARBON IN KUALA LUMPUR URBAN ENVIRONMENT AND ITS EFFECT ON HUMAN HEALTH

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ABSTRACT

Introduction: Polycyclic aromatic hydrocarbons (PAHs) in the ambient air have been categorised as priority pollutants due to their effect on human health. The presence of PAHs in the ambient particulate matter has been determined in several cities throughout the world. Kuala Lumpur is one of the major cities that has been affected by high concentrations of particulate matter and polycyclic PAHs as a result of various human activities.

Methodology: The concentrations of the 16 USEPA priority PAHs in different sizes of particulate matter in Kuala Lumpur have been measured using gas chromatography-mass spectrometry (GC–MS).

Results: The results indicate that the concentrations of PAHs predominated in particulate matter collected during biomass burning events. Local and regional sources including gasoline emissions;

natural gas and coal burning; biomass burning and diesel; and heavy oil combustion are major contributors to PAHs in the particulate matter. Total PAHs dominated by 5-ring and 6-

ring PAHs such as benzo[a]pyrene (BaP), indeno[1,2,3-cd]pyrene (IcP), benzo[b]fluoranthene (BbF), benzo[k]fluoranthene (BkF) and benzo[g,h,i]perylene (BgP). The cytotoxicity of the PAHs extract was assessed using the reduction of tetrazolium salts (MTT) test, which indicated that PAHs extracts collected during the SW monsoon are cytotoxic to V79-4 cells.

Conclusion: The total percentage of benzo(a)pyrene equivalent (BaP_{eq}) concentration in the fine particles was found to contribute to more than 50% of the potential health risk. The health risk assessment also revealed that the estimated incremental lifetime cancer risks (ILCRs) associated with BaP_{eq} exposure are negligible.

KEYWORDS: Seasonal variation, size-fractioned particulate matter, source apportionment, health risk assessment

[INV-9]

GENOTOXIC INTERACTIONS OF ENVIRONMENTAL POLLUTANTS, MALNUTRITION AND SARS-CoV-2 VIRUS MAY EXACERBATE THE COVID-19 PANDEMIC

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ABSTRACT

In this presentation I present current evidence suggesting that severity of COVID-19 disease may be increased by the interactive genotoxic effects of air-pollution, malnutrition and RNA virus infections. This is supported by evidence that (i) RNA viruses are a cause of chromosomal instability and micronuclei (MN), (ii) those individuals with high levels of lymphocyte MN have a weakened immune response and are more susceptible to RNA virus infection and (iii) both RNA virus infection and MN formation can induce inflammatory cytokine production. Based on these observations we propose a hypothesis that those who harbor elevated frequencies of MN within their cells are more prone to RNA virus infection and are more likely, through combined effects of leakage of self-DNA from MN and RNA from viruses, to escalate pro-inflammatory cytokine production via the cyclic GMP–AMP synthase (cGAS), stimulator of interferon genes (STING) and the Senescence Associated Secretory Phenotype (SASP) mechanisms to an extent that is unresolvable and therefore confers high risk of causing tissue damage by an excessive and overtly toxic immune response. The corollaries from this hypothesis are (i) those with abnormally high MN frequency are more prone to infection by RNA viruses; (ii) the extent of cytokine production and pro-inflammatory response to infection by RNA viruses is enhanced and possibly exceeds threshold levels that may be unresolvable in those with elevated MN levels; (iii) reduction of MN frequency by improving nutrition and life-style increases resistance to RNA virus infection and moderates inflammatory cytokine production to a level that is immunologically efficacious and survivable.

[INV-10]

ROLE OF ENDOGENOUS CYANIDE IN THE DETOXIFICATION OF SELENIUM

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ABSTRACT

Selenium (Se) has an ambivalent character for humans and animals, i.e., essential and toxic. Because of physicochemical properties of Se, it can form a carbon-Se bond through the metabolic pathway, and its biological and toxicological effects are markedly dependent on its chemical form. The identification of Se-containing metabolites is expected to provide important clues to elucidate the metabolic pathway of Se. As Se is essential but exists in a trace amount, the analyses of selenometabolome require massive amounts of samples, such as urine, tissues/organs, and blood. Contrary, studies of selenometabolome in cultured cells are limited. Hence, my research group attempted to examine selenometabolome in cultured cells by speciation analysis. When human hepatoma HepG2 cells were exposed to sodium selenite, an unknown Se metabolite was detected in the cytosolic fraction by HPLC-inductively coupled plasma mass spectrometry (LC-ICP-MS). The unknown Se metabolite was also detected in the mixture of HepG2 homogenate and sodium selenite in the presence of exogenous glutathione (GSH). The unknown Se metabolite was identified as selenocyanate by electrospray ionization mass spectrometry. Because exogenous cyanide increased the amount of selenocyanate in the mixture, selenocyanate seemed to be formed by the reaction between selenide, a product of the reduction of selenite, and endogenous cyanide. Rhodanase, an enzyme involved in thiocyanate synthesis, was not required for the formation of selenocyanate from selenide and endogenous cyanide. We proposed to name the effect of endogenous cyanide a reactive cyanide species (RCNS) likened to NO- and HS- of reactive nitrogen and sulfur species, respectively. Selenocyanate was less toxic to HepG2 cells than selenite or cyanide, suggesting that it was formed to reduce the toxicity of selenite. Namely, selenite was metabolized to selenocyanate to ameliorate its toxicity temporarily in cultured cells exposed to surplus selenite. The mechanisms underlying the production of endogenous cyanide will be discussed.

KEYWORDS: Selenium, selenocyanate, cyanide, ICP-MS, ESI-MS, speciation

[INV-11]
ESSENTIAL ROLE OF COMPUTATIONAL TOXICOLOGY IN OPTIMIZING DRUG DISCOVERY

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ABSTRACT

Computer-aided drug discovery/design methods have played a major role in the development of therapeutically important small molecules for over three decades. Computational toxicology via predictive modelling and simulations plays a critical role as the integrative approaches that rely upon alternatives to animal testing for toxicological research and chemical safety assessments and in reducing the failure rate of new drugs in pharmaceutical research and development. Using recently published computational regression analyses of *in vitro* and *in vivo* toxicology data, significant gaps remain in early safety screening paradigms. More strategic analyses of these data sets will allow for a better understanding of their domain of applicability and help identify those compounds that cause significant *in vivo* toxicity, but which are currently mis-predicted by in silico and *in vitro* models. This talk covers the topics ranging from quantitative structure–activity relationship (QSAR) and other *in silico* studies, to *in vitro* to *in vivo* extrapolation (IVIVE) methods, to application of next-generation sequencing and high-throughput screening (HTS) data, to the use of artificial intelligence (AI) and machine learning (ML) to model critical *in vivo* toxicity end points.

KEYWORDS: Structure–activity relationship (SAR), QSAR, predictive toxicology, investigative toxicology, computational toxicology

[INV-12]
ALTERNATIVE (NON-ANIMAL) TESTING STRATEGIES FOR EVALUATING DEVELOPMENTAL TOXICITY POTENCY OF HIGHLY COMPLEX PETROLEUM SUBSTANCES

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ABSTRACT

Testing for prenatal developmental toxicity is one of the most animal- and resource-intensive testing endpoints in the field of toxicology. Hence, the use of alternative *in vitro* assays may reduce animal experimentation and resources needed to study the developmental toxicity potencies of chemical substances including petroleum substances. Petroleum substances are highly complex materials (UVCBs*), comprising of hundreds to millions of different hydrocarbons including polycyclic aromatic compounds (PACs). Developmental toxicity as observed with some petroleum substances has been associated with the presence of 3- to 7-ring PACs in these substances. To investigate this hypothesis further, a series of petroleum substances extracts (varying in PAC content) and products containing no PACs were tested in the scientifically validated alternative assays for developmental toxicity namely the mouse embryonic stem cell test (EST) and the zebrafish embryotoxicity test (ZET). Results show that all PAC-containing petroleum substances extracts, induced concentration-dependent developmental toxicity as quantified in the EST and ZET (at non-cytotoxic concentrations), with their potency being proportional to their 3- to 7-ring PAC content. On the contrary, PAC-free extracts tested negative in both assays, further corroborating the above-mentioned hypothesis. *In vitro* potencies in both EST and ZET were compared to published *in vivo* developmental toxicity studies, and good correlations exist between them. To conclude, our findings show the applicability of alternative *in vitro* assays (i.e., EST and ZET) in combination with analytical data, to assess *in vitro* developmental toxicity potency of highly complex petroleum substances, and the role of PAC in the observed toxicity.

**UVCBs: substances of Unknown or Variable composition, Complex reaction products or Biological materials.*

KEYWORDS: Developmental toxicity; alternative assays; polycyclic aromatic compounds; UVCBs; petroleum substances

[INV-13]
ENVIRONMENTAL TOXICANTS AND METABOLIC DISORDERS: IMPACT ON REPRODUCTIVE HEALTH CONCERNS

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ABSTRACT

The environment may be contaminated with endocrine disrupting chemicals (EDCs) from a variety of different sources. They are most often found in the food, chemical, and product packaging sectors. EDC endangers individuals by targeting a range of body organs and systems, including the reproductive system. A variety of mechanisms, including activating estrogen receptors, nuclear receptors, and steroidal receptors, may be used to target the reproductive system. Di-n-butyl phthalate (DBP), a frequently used industrial chemical, was one of the EDCs that caused significant changes in the male reproductive system by suppressing testosterone production. DBP regulates almost 400 genes in Leydig cells, Sertoli cells, and gonocytes. Bisphenol A, Dichlorodiphenyltrichloroethane (DDT), and Vinclozolin affect uterine contraction in rats through Uterotonin (Prostaglandin F2α, Acetylcholine and Oxytocin) Pathways. Phytoestrogens found in human and animal diets (genistein and quercetin) may also be EDCs. Although these substances have a moderate affinity for binding to estrogen receptors and interfere with the fluid volume and receptivity growth of the uterus during the peri-implantation phase, they may have a negative effect on embryo implantation. Diabetes and obesity have been causally associated with EDC exposure. Low testosterone levels are often linked to diabetes, obesity, and metabolic syndrome.

KEYWORDS: Environmental toxicants, phytoestrogens, diabetes mellitus, obesity

[INV-14]

AMORPHOUS SILICA EXPOSURE IN THE DEVELOPMENT OF CHRONIC KIDNEY DISEASE OF UNKNOWN ETIOLOGY WITHIN AGRICULTURAL WORKERS

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ABSTRACT

Introduction: We have hypothesized that exposure to amorphous silica nanoparticles from sugarcane burning in developing countries contributes to an endemic kidney pathology in agricultural workers called chronic kidney disease of an unknown etiology (CKDu). Elemental analysis shows that sugarcane stalks contain a high percentage of amorphous silica (SiO_2) that are released as nano-sized silica particles into the environment during burning.

Methods: To determine if SiNPs are present in kidney biopsies from agricultural workers in Mexico and Central America, we utilized single particle inductively coupled plasma mass spectrometry (SP-ICP-MS). In addition, we used a human kidney proximal convoluted tubule (PCT) cell line (HK-2) to examine responses to sugarcane ash, silica-free ash, and sugarcane ash derived SiNPs at 0.25, 2.5, and 25 µg/mL.

Results: Using SP- ICP-MS, we identified SiNPs within digested sugarcane ash which ranged in size from 190-212 nm. In kidney tissue of agricultural workers, we identified the same representative SiNP population in CKDu patients. Despite not being directly cytotoxic to HK-2 cells at 24 hours, SiNPs were readily taken up and generated reactive oxygen species. Vimentin staining confirmed HK-2 cells underwent epithelial-mesenchymal transition (EMT) following treatment with SiNP and sugarcane ash but not with silica-free ash.

Conclusions: These findings demonstrate that SiNPs are present in kidney biopsies of agricultural workers and are capable of driving a fibrotic phenotype in PCT cells similar to what is observed in patients with CKDu.

KEYWORDS: Kidney; CKDu; tubular interstitial nephritis; silica; nanoparticle

[INV-15]
TOXICITY EVALUATION OF INHALED IRON OXIDE NANOPARTICLES WITH DIFFERENT SURFACE CHARGE POLARITIES AGAINST PULMONARY CELLS

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ABSTRACT

Introduction: Metal-based nanomaterials such as iron oxide nanoparticles (IONPs) have received wide attention to be developed for therapeutic applications against lung cancer. However, the toxicity effect of IONPs upon inhalation has not been well studied. This study attempted to evaluate the toxicity mechanism of IONPs with different surface charge polarities in lung cells.

Methodology: PEG-coated-IONPs and amine-coated-IOPNs at various concentrations (0.3 to 1.0 mg/mL) were nebulized onto the air-liquid interface Calu-3 cells using PARI nebulizer for 2 min. Different types of analysis such as measuring ATP content, apoptosis, MMP, cytochrome C and caspase were carried out to evaluate the toxicity of IONPs. The cellular uptake elucidation is performed using various endocytosis inhibitors (i.e chlorpromazine, wortmanin etc).

Results: Following the deposition of IONPs via nebulization, the lactate dehydrogenase data showed that the proliferation of Calu-3 was affected with the decreasing trend: positively charged amine-coated-IONPs (proliferation: 35.3 ± 1.2%) < negatively charged PEG-coated-IONPs (56.3 ± 0.6%). In addition, positively charged IONPs were more potent to affect the apoptosis, ATP content, MMP, cytochrome C and caspase 3 levels in Calu-3 cells compared to negatively charged IONPs. Both amine-coated IONPs and PEG-coated IONPs were dependent on clathrin-mediated endocytosis for internalization into Calu-3.

Conclusion: Positive charged IONPs were more pronounced in inducing toxicity effects in lung cells compared to negative charged IONPs.

KEYWORDS: Surface polarity; inhalation; toxicity; endocytosis; Calu-3

[INV-16]

PROTEOMICS ANALYSIS TO COMPARE THE TOXICOLOGICAL PATHWAYS OF SILVER NANOPARTICLE IN SKIN CARCINOMA CELL AND ZEBRAFISH EMBRYO

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ABSTRACT

Introduction: A proteomic approach as a part of system toxicology is useful in the adverse outcome pathway (AOP) framework. A proteomics analysis is powerful for comprehensively measuring the profiles of proteins within cells or tissues, therefore the toxicological pathways of toxic substances are identified. Although regulatory decisions on chemical safety are based on human and environmental protections, the collaborative data between humans and ecology are limited. To fill the gap between toxicological models, the molecular effects of silver nanoparticles (AgNP) were investigated in both human skin cells and zebrafish embryos.

Methodology: The comprehensive sets of differentially expressed proteins were identified by LC-MS/MS system and characterised by Progenesis® QI for Proteomics. The toxicological pathways were indicated by the STITCH algorithm, based on KEGG pathways enrichment analysis.

Results: The predominant toxicological pathway analysed from human skin cells was DNA damage, whereas oxidative stress was a major pathway in the zebrafish group. A similar protein pathway disrupted by AgNP in both models was the metabolic process, which is important to maintaining cellular homeostasis, as well as the development of zebrafish embryos.

Conclusion: The proteomic approach was promising to understand the underlying toxicological mechanisms of AgNP. The future study on transcriptomics or metabolomics would be constructive to this finding. The multi-omics would be powerful to screen the safety of other nanoparticles.

KEYWORDS: Silver nanoparticles; nanotoxicity; proteomics; adverse outcome pathway (AOP)

[INV-17]
IMPACTS OF DEVELOPMENTAL EXPOSURE TO PFAS ON HUMAN HEALTH: THE HOKKAIDO BIRTH COHORT STUDY

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ABSTRACT

The Hokkaido Study on Environment and Children's Health is an ongoing study consisting of two birth cohorts of different population sizes. Our primary objectives are to (1) examine the effects that low-level environmental chemical exposures have on birth outcomes, (2) follow the development of allergies, infectious diseases, and neurobehavioral developmental disorders, as well as perform a longitudinal observation of child development; and (3) identify high-risk groups based on genetic susceptibility to environmental chemicals. The purpose of my speech is to provide an update on the progress of the Hokkaido Study, summarize recent results, and suggest future directions.

The latest findings indicate maternal serum folate was not associated with birth defects under current folate intake levels. Prenatal chemical exposure and smoking were associated with birth size and growth, as well as cord blood biomarkers, such as adiponectin, thyroid, and reproductive hormones. We also found significant associations between the chemical levels and neurodevelopment, asthma, and allergies.

Longer follow-up for children is crucial in birth cohort studies to reinforce the Developmental Origins of the Health and Disease hypothesis. In contrast, considering shifts in the exposure levels due to regulation is also essential, which may also change the association to health outcomes. Our study found that individual susceptibility to adverse health effects depends on the genotype. Epigenome modification of DNA methylation was also discovered, indicating the necessity of examining molecular biology perspectives. International collaborations can add a new dimension to the current knowledge and provide novel discoveries in the future.

KEYWORDS: Per- and polyfluorinated alkyl substances (pfas); birth size; hormone; allergy and infectious diseases; epigenetics

[INV-18]

SAFETY OF HERBAL MEDICINE: THE SOUTHEAST ASIA SCENARIO

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ABSTRACT

Similar to pharmaceutical drugs, herbal medicine may also cause adverse effects. The high prevalence of herbal medicine uses in the Southeast Asia region contributed towards an increase in reports of adverse events across the past decade. A review on the regional scenario of herbal medicine pharmacovigilance was conducted by searching for related published articles and grey literature on adverse effects and pharmacovigilance of herbs in the different countries of Southeast Asia. Over the years, herbal products have been increasingly regulated with much diversity in the requirements for their quality in different countries. Studies indicated that the adverse events that were reported to be potentially related to herbal medicine could be due to the herb (single herb or mixed formulation) itself, adulteration, contamination, and herb drug interaction. The current national pharmacovigilance systems on herbal medicine of most countries rely on spontaneous reporting of adverse events. The reported adverse events were often multifaceted with renal or hepatic related effects being the most worrying. However, the establishment of a causal-relationship of such events with the intake of herbal medicine is challenging with spontaneous reporting and anecdotal data. Such gap in pharmacovigilance for herbal medicine needs to be further addressed and may be improved with active monitoring or further safety research. Pharmacovigilance of herbal medicine in the Southeast Asia region is still in its infancy though identification of commonly reported or serious adverse events as well as the herbs suspected to be related can instigate further analysis and actions.

KEYWORDS: Herbal medicine, adverse events, Southeast Asia, pharmacovigilance

[INV-19]
CLINICAL TOXINOLOGY AND ITS DEVELOPMENT AND PROGRESS IN MALAYSIA

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ABSTRACT

Clinical Toxinology has been established as one of the Special Interest Group under The College of Emergency Physicians (CEP), Malaysia since 9th of March 2022. It is a specialised area of clinical medicine focused on the pathophysiology, diagnosis, treatment and prevention of diseases caused by animals, plants, mushrooms and bacteria. It encompasses a broad range of medical conditions resulting from envenomation by venomous terrestrial and marine organisms, and also poisoning from ingestion of animal and plant toxins. In recent years, the field of toxinology has expanded substantially. On one hand it studies venomous animals, plants and microorganisms in detail to understand their mode of action on targets. While on the other, it explores the biochemical composition, genomics and proteomics of toxins and venoms to understand their three interactions with life forms (especially humans), development of antidotes and exploring their pharmacological potential. The speaker will highlight its development and progress in Malaysia over the past few years.

KEYWORDS: Clinical toxinology; Malaysia; RECS; envenomation; poisoning

[INV-20]

DIET, GENOMIC STABILITY AND RELATIVE CANCER RISK : WHERE MALAYSIA STANDS?

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ABSTRACT

The incidence of cancer globally is increasing, partly due to lifestyle factors. Despite a better understanding of cancer biology and advancement in cancer management and therapies, current strategies in cancer treatment remain costly and cause socioeconomic burden especially in Asian countries. Hence, instead of putting more efforts in searches for new cancer cures, attention has now shifted to understanding how to mitigate cancer risk by modulating lifestyle factors. It has been established that carcinogenesis is multifactorial, and the important detrimental role of oxidative stress, chronic inflammation, and genomic instability is evident. To date, there is no study linking dietary pattern and genomic stability in cancer risk in the Asian food landscape. Malaysia, on the other hand has very limited studies related to this field of interest. Thus, this presentation will focus on how diet and cancer are related, carcinogens in food product, and recent literature on dietary pattern and genomic stability and its relationship with cancer risk in Asia, including Malaysia.

LIST OF ORAL PRESENTERS

[REG-1]

OECD QSAR TOOLBOX SCREENING OF TOXICITY ENDPOINTS OF CHEMICALS IN RESEARCH AND DEVELOPMENT (R&D)

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ABSTRACT

Introduction: Polyol esters (PE) and sugar-based surfactants alkyl polyglycosides (APG) have attracted considerable interest in the personal care applications as they are often labelled "eco-friendly". The derivatisation of PE and APG is being pursued to enhance their performance, and they are screened for toxicity properties to ensure suitability for the intended applications. Driven by the United Nations Sustainable Development Goals (UNSDGs) and the increasing global demand for non-animal tests in the safety evaluation of chemicals in various applications, PETRONAS is embedding both *in-silico* predictive and *in vitro* toxicology in its R&D of new products/materials.

Methodology: The predictions of mutagenicity, skin/eye irritancy/corrosivity, and skin sensitization were by way of read-across of experimental data of analogues, using the Automated Workflow (AW) and Standardized Workflow (SW) of the OECD QSAR Toolbox. The methods predict properties associated with the toxic effects of chemicals based on functional groups and mechanisms of action.

Results: The predicted results for PE are consistent with the *in vitro* tests for the four endpoints, while for APG are currently a work in progress. Preliminary results shows that the predicted value for skin sensitization is positive whist the *in vitro* results were inconclusive which may be attributed to the UVCB (Unknown or Variable Composition, Complex reaction products, or Biological Materials) characteristics.

Conclusion: In summary, the reliability of desktop assessment for toxicity evaluation of a chemical is depending on the characteristics of the tested chemicals. For UVCBs, licensed software is needed to complement the public domain Toolbox in generating a comprehensive prediction.

KEYWORDS: Non-animal methods; product safety evaluation; OECD QSAR toolbox; OECD guidelines; product research & development

[NAT-1]

ASSESSING THE TOXICITY OF SIBUTRAMINE CHLORIDE-ADULTERATED WEIGHT LOSS SUPPLEMENTS IN RATS

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ABSTRACT

Introduction: Weight-loss supplements are often natural or herbal supplements designed to promote weight loss and health improvement. However, the increase of consumption leads to the fraudulent adulteration with conventional pharmaceutical drugs, including sibutramine chloride. This study was conducted to analyse the toxicity effect of sibutramine chloride-adulterated weight loss supplements in rats.

Methodology: On the basis of a report by The National Agency for Drug and Food Control, Republic of Indonesia (BPOM RI), six samples of sibutramine chloride-adulterated weight loss supplements (J1-J6) were collected from an online market. The samples' toxicity was evaluated using 42 male Wistar rats. The rats were separated into seven samples: control, J1, J2, J3, J4, J5, and J6. The effects of toxicity were evaluated for 35 days. The rats body weight were observed weekly to monitor the weight loss. To determine the toxicity of the samples, liver weight, kidney weights, urine pH, uric acid level, albumin, urea, creatinine, Serum Glutamic Oxaloacetic Transaminase (SGOT), Serum Glutamic Pyruvic Transaminase (SGPT), Alkaline Phosphatase (ALP), Gamma-glutamyl transferase (GGT), bilirubin levels were measured on day 36.

Results: The J1 supplement caused rats to lose weight the quickest when compared to other supplements tested. The kidney and liver weights of rats given sibutramine chloride-adulterated weight loss supplements were greater than those of rats in the control group. J1 indicated the most toxic supplement among six others. The J1-treated group displayed the highest levels of toxicity for all evaluated parameters. Our results are consistent with the summaries of previous studies that would be essential for a rigorous hazard and risk assessment of weight loss supplements adulterated with sibutramine chloride.

Conclusion: Considering further investigation of sibutramine chloride adulteration in weight loss supplements would be of use to ensure consumer safety.

KEYWORDS: Adulteration, toxicity, sibutramine chloride, weight loss supplements

[NAT-2]

ASSESSMENT OF WOUND HEALING POTENTIAL USING *Eleusine indica (Linn.) Gaertn* LEAVES EXTRACT ON SPRAGUE DAWLEY RATS

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ABSTRACT

Introduction: As the cost of wound treatment has been increasing over the years, there is a need to find an alternative to solve the issue. *Eleusine indica (Linn.) Gaertn* or *rumput sambau* is proposed in this study. The plant has been used as a local traditional wound healing remedy, but its effectiveness is not yet reported.

Methodology: *E. indica* cold infusion extract was prepared using the maceration technique and dried using freeze dryer. 120 male Sprague Dawley rats were divided into four main groups. The treated group received 1.5% and 3% *E. indica* topically, Intrasite® gel as the positive control and PBS solution as the negative control. A total of six full-thickness wounds were induced on the dorsal part of the skin. The study period was 14 days, and six from each group were sacrificed on days 1, 3, 6, 10 and 14. Parameters studied included macroscopic observation of the wound, biochemical (protein) and histological observation with Hematoxylin and Eosin (H&E) and Masson's Trichrome staining.

Results: The percentage of wound healing based on wound surface area for the treatment of 3% of *E. indica* showed a significant difference compared to the control group on the first and third days ($p < 0.05$). The protein level for 1.5% *E. indica* treatment showed a significant increase from day 3 to day 6 ($p < 0.05$) compared to the first day. Histological observation found that the *E. indica* showed increased infiltration of inflammatory cells during the inflammatory phase and dense collagen distribution.

Conclusion: The study recommended the effectiveness of *E. indica* as a wound-healing agent based on the evidence provided by the open wound of the rats.

KEYWORDS: *Eleusine indica*, wound healing, rats, extraction, histology, protein

[NAT-3]
PRESENCE OF PYRROLIZIDINE ALKALOIDS IN REGISTERED NATURAL PRODUCTS IN MALAYSIA

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ABSTRACT

Introduction: Phytochemicals are secondary metabolites produced by plants as defense mechanism or to aid reproduction. While phytochemicals exhibit pharmacological activities important for health and drug discovery, several phytochemicals are toxic and potentially carcinogenic, such as pyrrolizidine alkaloids (PAs), which are heterocyclic phytochemicals produced by more than 6000 plant species. Riddelline, senecionine, lasiocarpine, heliotrine, seneciphylline, lycopsamine, clivorine, and monocrotaline are some of the compounds within this group, with lasiocarpine, monocrotaline and riddelliine classified as 2B carcinogens. PAs are hepatotoxic, genotoxic, mutagenic and hepatocarcinogenic. Plants known to contain PAs typically grow as weeds and contaminate foodstuffs including grains, milk, honey and eggs, as well as plants used as tea, supplements and medicines.

Methodology: By using an official online database, QUEST3+, the number of natural products registered in Malaysia containing plants species reported to contain PAs were generated. These include plants in various genera known to produce PAs such as Senecio, Borago, Lithospermum, Heliotropium, Eupatorium, Tussilago and Symphytum.

Results: The search identified 135 registered natural products with PA producing plants as ingredient; 78 products containing *T. farfara,* 33 products containing *B. officinalis,* 14 products containing *A. capillaris, 6* products containing *Gynura spp,* 2 products containing *E. perfoliatum,* 1 product containing *P. japonicus* and 1 product containing *A. conyzoides.*

Conclusion: Malaysians could be exposed to genotoxic and carcinogenic PAs through consumption of natural products, thus increasing the risk of developing cancers. Thus, it is important to assess the risk of PAs in natural products, in order to ensure the public health safety.

KEYWORDS: Pyrrolizidine alkaloids, natural products, hepatotoxic, genotoxic, carcinogenic

[NAT-4]

NMR-METABOLOMICS: THERAPEUTIC POTENTIAL OF FERMENTED SOYBEAN EXTRACT AGAINST LEAD (PB) TOXICITY USING ZEBRAFISH MODEL

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ABSTRACT

Introduction: Lead (Pb), even in small quantity, is detrimental to multiple body systems. Chelator such as dimercaptosuccinic acid (DMSA) is used to treat Pb toxicity, yet it also gives various negative side effects. Fermented soybean (tempeh) that is known having high antioxidant effect might potentially be useful in alleviation of lead toxicity. This study assessed the therapeutic potential of fermented soybean extracts (FSE) against Pb toxicity in a zebrafish model.

Methodology: The Pb and FSE concentrations were preliminary investigated before studying the therapeutic effect of FSE against Pb toxicity. All results were evaluated using NMR metabolomics with additional support of open field test and transmission electron microscope (TEM) analysis.

Results: Preliminarily studies showed that Pb inducement significantly altered the behaviour of zebrafish, and the 27 differential metabolites were increased and decreased in low (5 mg/L) and high (10 mg/ L) Pb concentrations, respectively when compared to the control. Whereas zebrafish that exposed to 50 mg/L FSE significantly changed four metabolites namely glucose, isoleucine, sn-glycero-3-phosphocholine, and glutamine. Zebrafish that exposed to 300 mg/L FSE presented a necrosis-like cell death in the TEM result. In therapeutic study, four key differential metabolites (glutamine, glutamate, glutathione, and taurine) were significantly upregulated in FSE-treated (50mg/L) Pb-induced zebrafish. While citrulline was significantly upregulated only in Pb-induced group without any treatment.

Conclusion: These results suggested that even though the treatment groups (FSE and DMSA) did not normalize, but FSE potentially has retrieved the effect of Pb toxicity in this fish model.

KEYWORDS: Pb poisoning; fermented soybean; zebrafish; NMR metabolomics

[NAT-5]

TOXICITY OF PIPER SARMENTOSUM LEAF EXTRACT IN DIFFERENT SOLVENT SYSTEMS AGAINST ZEBRAFISH (DANIO RERIO) EMBRYOS

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ABSTRACT

Introduction: *Piper sarmentosum (P. sarmentosum),* is a creeping herb with pungent odour known as Kaduk that is commonly consumed as vegetable staples in Malaysia due to its myriad potential pharmacological activities. However, little is known on the toxicity effects of *P. sarmentosum* leaf extracts. The present study evaluates the toxicity effects of *P. sarmentosum* extract procured from the leaves, using four different solvents commonly used to extract active phytochemical compounds against the embryonic development of *Danio rerio* (zebrafish).

Results: In the present study, leaf extracts of *P. sarmentosum* were obtained from hexane (HE), dichloromethane (DE), ethyl acetate (EA) and methanol (ME). The phytochemical screening of all extracts were conducted using GC-MS. Toxicological assessment of all extracts on zebrafish embryonic developmental stages (survival, hatching and heart rates, and morphological changes) was recorded daily for up to 96 hours post-fertilization (hpf).

Results: ME has the highest percentage yield of 14.73%, followed by EE, HE, and DE with percentage yields of 6.38, 5.50 and 2.30%, respectively. The phytochemical screening by GC-MS revealed prominent compounds that possess toxicity and contribute to the toxicity effects of the solvent extracts. HE exhibited the highest mortality rate at 96 hpf with LC_{50} value of 23.33 ppm, followed by DE, EE and ME with LC_{50} value of 25.60 ppm, 32.31 ppm and 70.25 ppm, respectively. The present study demonstrated a significant slow heart rate, decreased hatching rate, lack of tail extension and somite formation, with presence of scoliosis and edema in treated embryos, which further postulates the acute toxicity of HE, among other solvent extracts.

Conclusion: These findings revealed the toxicity of *P. sarmentosum* leaf extract on living organism, which was highly influenced by the solvents, concentration and time exposure employed.

KEYWORDSs: *Piper sarmentosum,* zebrafish embryo, toxicity, solvent extraction, asarone

[MED-1]
EFFECTS OF 2-AMINO-1-METHYL-6-PHENYLIMIDAZO[4,5-B]PYRIDINE (PHIP) ON RWPE-1 CELL LINE

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ABSTRACT

Introduction: 2-Amino-l-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) is the most abundant type of heterocyclic amines found in cooked meat. This compound is formed through heat-dependent condensation of creatinine, phenylalanine and sugar, and varies with food type and cooking conditions. The objective of this study is to evaluate the effects of PhIP on normal prostate cell line, RWPE-1, at human exposure level.

Methodology: The cells were treated with different concentrations of PhIP ranging from 10^{-10} - 10^{-7}M, which were diluted in 0.003% DMSO. The experiment was carried out with or without pooled human liver microsomes as bioactivation system. Cell proliferation effects of PhIP on normal prostate cell line, RWPE-1 were determined using MTS assay. Cell transformation and invasion assays were carried out to assess its carcinogenic transformation.

Results: Three of the PhIP concentrations were able to induce RWPE-1 cell proliferation in the presence of metabolic activation system. In cell transformation assay, cells treated with all concentrations of PhIP in the presence of metabolic activation system showed anchorage-independent growth with the most prominent result observed in those treated with 10^{-7}M PhIP. However, these cells did not possess any invasive properties.

Conclusion: PhIP is able to induce neoplastic transformation in normal human prostate cell line, RWPE-1, at human exposure level.

KEYWORDS: Food carcinogen, PhIP, prostate cells, cancer, *in vitro*

[MED-2]
TOXICITY OF STREPTOZOTOCIN ON RETINAL MICRO-ANATOMICAL CHANGES IN DIABETIC MICE

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ABSTRACT

Introduction: Retinal damage is common with a chronic condition of diabetes mellitus. The elevated blood sugar levels alter the multiple biochemical pathways like the polyol pathway and advanced glycation end product pathways. Moreover, neuroanatomical and microvascular anatomical changes are common in diabetic conditions. Though, the exact anatomical changes of the retina with localized actions of streptozotocin (STZ) toxicity are not explored yet in mice. The present study was designed to investigate the localized toxicity actions of STZ in micro-anatomical changes of the retina in diabetic mice.

Methodology: Diabetic mice were developed with intraperitoneal administration of STZ (35 mg/kg). The localized intravitreal (*i.vit.*) administration of STZ (20 µl of 7% STZ) was made on the 7th day in diabetic mice. Thereafter, mice were sacrificed on 21 days of STZ *i.vit.* treatments. The micro-anatomical changes of the retina were assessed by histopathological methods.

Results: The *i.vit.* administration of STZ was shown potential micro-anatomical changes in retinal tissue when compared to the retina of normal mice.

Conclusion: STZ-associated micro-anatomical changes can lead to the potential uses of animal models for the therapeutic evaluation of various retinal protective agents and ophthalmic drugs. Further, it is open Pandora's Box for the newer toxin model development for the preclinical evaluation.

KEYWORDS: Extravasation, intravitreal injection, neurovascular complication, retinal degeneration, vacuolations

[MED-3]
PATHOPHYSIOLOGICAL PERSPECTIVE OF ALUMINIUM CHLORIDE-INDUCED NEUROVASCULAR TOXICITY IN RATS

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ABSTRACT

Introduction: Heavy metal like aluminium is mostly engaged in the changes of cerebrovascular system. Exposure to aluminium ions in the human body is quite common and it raises the risk of neurovascular complications like stroke. Aluminium exposure could enhance the risk of stroke via a homocysteine-mediated pathway and cause neurovascular diseases like vascular dementia, however, there is a lack of knowledge in this regard. Hence, this study was performed to understand the pathophysiology of aluminium chloride-induced neurovascular toxicity in rats.

Methodology: Aluminium chloride at the dose of 150 mg/kg/ip was administered daily for 7 days to the rats. Later, these rats were kept untreated for the next 21 days to gradually develop the neurovascular disease. Plasma homocysteine levels were estimated, and the rat's brain coronal section were stained with hematoxylin-eosin for histopathological analysis.

Results: Plasma homocysteine levels were found to be significantly high in the aluminium chloride-treated rats. These indicate that aluminium chloride has affected the neurovascular system functioning through the homocysteine-mediated pathway. Moreover, histopathological findings revealed significant neuronal damage in different areas of the hippocampus which further reinforces the neurovascular dysfunction.

Conclusion: These study findings conclude that aluminium chloride induces hyperhomocysteinemia and causes damage to the neurovascular system. Moreover, this condition if left untreated can lead to neurodegeneration, perhaps causing vascular dementia. Hence, these study findings add new knowledge to understanding the pathophysiology behind aluminium chloride's toxic effects in developing a neurovascular disease like vascular dementia.

KEYWORDS: Aluminium chloride, homocysteine, neurovascular toxicity, *Rattus norvegicus*, vascular dementia

[MED-4]
STREPTOZOTOCIN TOXICITY IN MICE RETINAL LAYER FUNCTION

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ABSTRACT

Introduction: The dysfunction of the retinal layer is observed in the retinopathy condition. Certain drugs are known to cause retinal damage like chlorpromazine, quinolones, thioridazine, deferoxamine, topiramate, metronidazole, latanoprost, epinephrine, niacin, rosiglitazone, tamoxifen, canthaxanthin, talc. Streptozotocin (STZ) is one of the naturally occurring (*Streptomyces achromogenes*) alkylating agents and it causes retinal neural degeneration via the expression of vascular endothelial growth factor and their receptors. However, the exact functional changes and cholinergic changes in the retinal layer are not investigated with neurovascular toxins *i.e.,* streptozotocin. The present study is designed to investigate the role of STZ toxicity in retinal layer-associated visual functions with the influence of cholinergic transmission in neurovascular tissue in diabetic mice.

Methods: Diabetic mice were developed with intraperitoneal administration of STZ (35 mg/kg; day 1). Then, intravitreal STZ (20 µl of 7% STZ; *i.vit.*) injection was made on the 7th day. The retinal layer function was assessed by visual cue method using Morris water-maze (MWM) device on 0, 7, 14, and 21st days. The changes in cholinergic neurotransmitters were assessed by estimation of acetylcholinesterase (AChE) activity in retinal tissue.

Results: The STZ causes the diabetic mice via elevation of blood glucose levels greater than 150 mg/dl. Besides, *i.vit.* administration of STZ was declined retinal layer functions along with modulation of AChE activity levels.

Conclusion: STZ causes the retinal layer dysfunction via modulation of cholinergic neurotransmission in neurovascular tissue of the retina.

KEYWORDS: Acetylcholinesterase, macular degeneration, neurotransmitter, retinal microvascular tissue, visual cue function

[MED-5]
POTENTIAL TOXIC EFFECTS OF STREPTOZOTOCIN ON VASCULAR SYSTEM IN RATS

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ABSTRACT

Introduction: The prevalence of diabetes mellitus is on the rise, especially in developing nations like Southeast Asia. More robust research is conducted in this aspect. One of the commonest models for investigating diabetes mellitus is streptozotocin induced diabetes in rodents. Streptozotocin is well known for its selective toxicity towards pancreatic beta cells which makes it a suitable candidate to induce diabetes with a similar pathophysiological profile observed in humans. Nevertheless, there are reports on the effects of streptozotocin on other systems. Hence, we would like to investigate the toxic effects of streptozotocin on the vascular system using rats.

Methodology: Male Sprague Dawley rats were used in this study. They were distributed into normal control or streptozotocin groups. Streptozotocin was administered at a dose of 50 mg/kg once intraperitoneally. The rats were observed for 21 days and endothelial nitric oxide synthase (brain) as well as homocysteine (plasma and brain) were estimated at the end of study.

Results: Endothelial nitric oxide synthase level was significantly lower while homocysteine levels were significantly higher in streptozotocin group relative to normal control group. This implies that streptozotocin has an impact on the vascular system by regulating the levels of both endothelial nitric oxide synthase and homocysteine.

Conclusion: Streptozotocin caused alteration of endothelial nitric oxide and homocysteine levels. This finding adds new insight and creates a new area of research to better understand the effects streptozotocin have on the vascular system. It is worthwhile to further investigate the effects of streptozotocin on other vascular parameters or even other systems.

KEYWORDS: **Endothelial nitric oxide synthase, homocysteine, nitric oxide, streptozotocin, vascular dysfunction**

[ENV-1]
DETECTION OF MYCOTOXINS IN OLD BUILDINGS: OCCUPATIONAL EXPOSURE AND HEALTH RISK ASSESSMENT

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ABSTRACT

Introduction: Mycotoxins are secondary metabolites released by filamentous fungi and moulds that may negatively impact the building occupants' health. This study was to investigate the relationship between the prevalence of mycotoxins and the environment risk among the building occupants. This study was to investigate the relationship between the prevalence of mycotoxins and the environment risk among the building occupants.

Methodology: Building materials scrapped from ceilings and walls, and indoor air in two old buildings (Institute for Medical Research, IMR and Universiti Sains Malaysia, USM) were collected. Forty nine building occupants who had spent 5 to 9 hours in indoor environment were recruited. Liquid chromatography-tandem mass spectrometry (LC-MS/MS) was used to determine the level of mycotoxins with solid phase extraction (SPE) and polyethyleneimine bonded silica gel columns (PEI) as the extraction and clean-up methods.

Result: Asthma is the most common disease found among the building occupants, and 53% of the respondents reported that it may attribute to the environment condition. The LC-MS/MS results revealed sterigmatosystin and aflatoxin were identified in the old buildings. Building material samples had higher mycotoxin levels than those from indoor air, and highest levels of sterigmatocystin and aflatoxin were demonstrated in USM.

Conclusion: There was no significant threat to the health of the building occupants according to health risk assessment methods.

KEYWORDS: Old building, mycotoxins, indoor air, health risk, liquid chromatography-mass spectrometry (LC-MS/MS)

[ENV-2]

SYNTHESIS OF PHOSPHANECOPPER(I) BENZOYLTHIOUREA COMPLEXES AND THEIR ACUTE TOXICITY STUDIES IN EMBRYO OF ZEBRAFISH

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ABSTRACT

Introduction: Phosphanecopper(I) thiourea, biologically, had shown the potential to be a good antimicrobial agent. However, excessive release of these compounds may cause harm and pollution to the aquatic life, water system and the environment. Therefore, we determined the toxicity level of the compounds and examined their effect on the embryos of zebrafish.

Methodology: Several benzoylthiourea ligands (L1-L2) and phosphanecopper(I) benzoylthiourea complexes (C1-C4) were synthesized and characterized using spectroscopic and analytical methods. Each of the compounds was tested for their toxicity via zebrafish embryos test (FET) at five different concentrations. The embryos were observed at 24, 48, 72 and 96 hpf for their core endpoints and behavioural response towards those concentrations of compounds. Embryos treated in 4 mg/L dichloroaniline and 0.5% DMSO were used as positive control and solvent control while untreated embryos were used as negative control.

Results: Various acute toxicity levels were observed for tested compounds. Zebrafish embryos were observed to have normal development though has been exposed to N-[[bis(2-hydroxyethyl)amino]thioxomethyl]-benzamide (L1) ligand at a high concentration of 1600 uM. Besides, at doses not exceeding 6.25 µM and 1.5625 µM, C2 and C3 were not toxic to 96-hpf zebrafish embryos. Meanwhile, the development of zebrafish embryos and their hatching rate were affected when tested with a high concentration of the other ligands and complexes.

Conclusions: This study identified the toxicity and the effects of synthesized benzoylthiourea ligands and phosphanecopper(I) benzoylthiourea complexes on the embryos of zebrafish, but further and intense tests are required to further confirm this study.

KEYWORDS: Toxicity, embryos, copper, phosphine, benzoylthiourea

[ENV-3]
EXPOSURE TO DIOXINS FROM PEATLAND FIRES INDUCES OXIDATIVE DNA AMONG FIRE-FIGHTERS IN MALAYSIA

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ABSTRACT

Introduction: Peatland fire common occurs during the hot season in Southeast Asian countries including Malaysia. Annually, the Malaysian Fire & Rescue Department receive at least 1,500 calls relating to open-burning particularly during the El Niño season. Combatting peatland fire is a lengthy process involving a large participation of the fire squad. Consequently, exposure to cancerous chemicals, specifically dioxins, to the fire-fighters is very high. This study examines the level of 17 congeners of dioxin/furan and its correlation with the level of oxidative stress biomarkers, 8-OHdG in the blood serum of the fire-fighters.

Methodology: Forty-two fire-fighters from five states in Malaysia identified as having involved with peatland fire extinguishing consented to donate 10 mL of their whole blood taken from cubital fossa. The blood samples were spun at 2,500G for 15 minutes and the separated serum were extracted using Accelerated Solvent Extraction method for analysis of 17 dioxin/furan congeners. A 20µL serum from each sample was drawn for oxidative stress biomarker analysis using enzyme-linked immunosorbent assay (ELISA) and its association with dioxins level.

Results: The concentrations of dioxin/furan range between 0.55 pg/g serum lipid to 150.91 pg/g serum lipid. The geometric mean concentration of the most toxic congeners, 2,3,7,8-TCDD is 0.045 pg/g WHO_{2005}TEQ serum lipid whereas the controlled and exposed group are 7.41±5.62 pg/g serum lipid and 15.58±37.64 pg/g serum lipid, respectively. Significantly important, the median (iqr) of the 8-OHdG concentration level detected is 13.00 (20.62) ng/mL ranging between 3.83 ng/mL to 101.00 ng/mL.

Conclusion: The study establishes that fire-fighters extinguishing peatland fires are potentially exposed to dioxin/furan that elevates the 8-OHdG level.

KEYWORDS: Peatland fire; fire-fighters; dioxins; 8-OHdG; occupational exposure

[ENV-4]
POLYCHLORINATED DIBENZO-P-DIOXINS AND DIBENZOFURANS (PCDD/FS) OCCURRENCE AND PROFILES IN MALAYSIAN PEAT

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ABSTRACT

Introduction: PCDD/Fs are highly toxic and persistent pollutants in the environment. They are produced as a byproduct of combustion of organic materials. Peat is often susceptible to fire especially during drought seasons although it is usually associated with anthropogenic activities. Peat burning has resulted in large loss of carbon storage and production of toxic emissions including PCDD/Fs. The objective of this study is to determine the occurrence of PCDD/Fs in Malaysian peat.

Methodology: 34 peat samples from four states in Malaysia – Pahang, Johor, Selangor and Terengganu were collected at two to five different depths (surface, 0-50 cm, 51-100 cm, 101-150 cm and 151-200 cm). These samples were then dried, extracted, purified and subjected to analysis for PCDD/Fs using GC-HRMS.

Results: Surface peat at different locations always showed the highest amount of PCDD/Fs when compared to other depths notwithstanding the area from which they were collected nor history of previous burn. This occurred predominantly due to surface deposition of PCDD/Fs from air. The range of total PCDD/Fs detected amongst the samples analysed are 0.3529 pg WHO_{05}-TEQ g^{-1} to 56.7310 pg WHO_{05}-TEQ g^{-1} which is way below the 1200 pg WHO_{05}-TEQ g^{-1} limit set by WHO. It is observed that the most toxic form of PCDD/Fs –2,3,7,8-tetrachlorodibenzo-p-dioxin, also present in some of the samples.

Conclusion: In this study, the level of PCDD/Fs in peat samples demonstrated no significant threat to human health. However, caution needed as peat burning may produce larger amounts of PCDD/Fs as peat soil contains higher amounts of organic matter which plays an important role in PCDD/Fs formation.

KEYWORDS: PCDD/Fs, peat fire, occurrence, profile, air pollution

[ENV-5]
HEAVY METALS IN BAUXITE: A SUMMARY OF TOXICOLOGICAL IMPLICATIONS ON COMMUNITIES IN BUKIT GOH, KUANTAN

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ABSTRACT

Introduction: Bauxite mining activities in Felda Bukit Goh, Kuantan, Pahang, has been operated since early 2013. The communities in the vicinity were exposed to hazardous heavy metals from the mining activities. Therefore, the objectives of this paper were to summarise the toxicology of selected heavy metal levels (As, Cd, Cr, Ni, Pb and Al) from the bauxite dust in areas located close to the mines.

Methodology: Various cross-sectional studies were conducted on randomly selected adults and school children. Data from respondents' background and their health symptoms were obtained using self-constructed questionnaires to collect information Environmental sampling for school indoor air were carried out. All of the air samples were analyzed using Inductively Coupled Plasma-Mass Spectrometry (ICP-MS).

Result: From the environmental air monitoring in 2015, the PM10 levels were above the standards in the selected households and in 2016 it was found that the PM10 level in classroom dust was below the Malaysian standard, however, the heavy metals levels were high. In 2015, for acute toxic health effects, the prevalence of respiratory reported symptoms as well as the dermal reported symptoms were high. Cr and Ni could be the contributing factors to dermal reported symptoms. Survey in 2016, stated that cough**,** runny nose and nasal congestion were still high in the previous 12 months. As for chronic toxic health effects on the school children's health includes, impairment in neurobehavioral performance, reduction in lung functions capability, and high levels of heavy metals in their hair and nails.

Keywords: Bauxite mining, heavy metals toxicity, respiratory symptoms, dermal symptoms

[ENV-6]
PESTICIDE USAGE AND CHOLINESTERASE ENZYME INHIBITION IN FARMERS OF SELECTED SITES OF BHUTAN

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ABSTRACT

Introduction: An estimated 69% of the population of Bhutan is engaged in agriculture farming. Farmers are exposed to a wide variety of pesticides during the formulation, preparation, transport, storage, mixing and application of pesticides posing a significant health risk. A case-controlled cross-sectional study of farmers in selected sites of Bhutan was conducted to characterize the level of exposure to pesticides and assess the clinical symptoms associated with the exposure.

Methodology: A total of 399 participants were enrolled in the study comprising of 295 exposed farmers and 104 healthy and unexposed controls. A structured investigator administered questionnaires were used to assess their exposure and blood samples were taken for measuring acetylcholinesterase activity level.

Results: There was a significant difference between the AChE enzyme inhibition of exposed and non-exposed control groups (652.01 vs 733.68) observed in the study ($P < 0.001$). Of the total of 295 farmers, 62 (21.01%) had severe acetylcholinesterase enzyme inhibition of >30% as compared to the unexposed group. The most common symptoms reported were headache (OR 1.08, 0.60-1.93) and neurological problems like forgetfulness, lack of concentration (OR 1.12, 0.50-2.48) and increased tiredness (OR 1.075, 0.52-2.19) that were significantly associated with the AChE enzyme inhibition.

Conclusion: This pilot study provides indication of exposure to pesticides in the selected sites of the country. Furthermore, it provides evidence for future work by identifying the exposure patterns and pathways of individuals most at risk in the farming communities of the country. Surveillance and bio-monitoring programs are instantly required.

KEYWORDS: Acetylcholinesterase, Bhutan, farmers, occupational exposure, pesticides.

[ENV-7]

THE MOLECULAR MECHANISM OF TRIPHENYLTIN(IV) DIISOPROPYLDITHIOCARBAMATE-INDUCES CYTOTOXICITY IN K562 HUMAN ERYTHROLEUKAEMIA CELLS

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ABSTRACT

Introduction: The novel di-and tri-phenyltin(IV) dithiocarbamate compounds represented as R_nSnL_2 (where R=C_4H_9, C_6H_5; n= 2,3; L= *N*,*N*-dithiocarbamate), Ph_2Sn(*N*,*N*-diisopropyldithiocarbamate) (**OC1**), Ph_3Sn(*N*,*N*-diisopropyldithiocarbamate) (**OC2**), Ph_2Sn(*N*,*N*-diallyldithiocarbamate) (**OC3**), Ph_3Sn(*N*,*N*-diallyldithiocarbamate) (**OC4**), and Ph_2Sn(*N*,*N*-diethyldithiocarbamate) (**OC5**) were assessed for their cytotoxicity in K562 cells.

Methodology: The cytotoxicity and the mode of cell death were determined via MTT assay and Annexin V-FITC/PI assay, respectively. Cell cycle analysis was then conducted to identify the disturbance in cell cycle progression. The genotoxicity and the loss of mitochondrial membrane potential were determined via TMRE staining assay and Alkaline Comet assay, respectively. Next, the role of oxidative stress was rationalized via DHE staining assay, NAC assay and GSH assay. The caspase cascade activation was further determined via caspase-9, -8 and -3 activation assay. Finally, the cytotoxicity-associated protein expressions were confirmed through western blot analysis.

Results: All compounds inhibited the cells' growth at low micromolar concentrations (0.55-1.1 μM) and about 46-69% apoptotic events were induced at their respective IC_{50} doses. **OC2**, which showed the most promising antiproliferative activity, was selected for further analyses. The results demonstrated that **OC2** induced mitochondria-mediated apoptosis triggered upon DNA damage, followed by, the accumulation of ROS and caspase cascade activation as well as cleaved-PARP. The role of oxidative stress was corroborated by the significant reduction in GSH levels and percentage of apoptosis in NAC-pretreated cells. Besides, inducible p21 expression of **OC2** caused cell cycle arrest in the S phase.

Conclusion: OC2 demonstrated the most potent antileukemic activity in K562 cells by inducing mitochondria mediated-apoptosis and arresting cell cycle distribution.

KEYWORDS: Organotin, apoptosis, cell cycle, caspase cascade, genotoxicity

[ADV-1]

DIOXINS EMISSION PREDICTION FROM PEAT SOIL USING ARTIFICIAL NEURAL NETWORKS (ANN)

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ABSTRACT

Introduction: Dioxins are formed as unintentional by-products from combustion process, especially from incomplete combustion. This highly toxic pollutant is harmful to human health and environment. Malaysian peat is commonly acidic or extremely acidic suggesting high chlorine and/or other organic acid contents which play an important role as the catalysts or precursors in dioxins formation. This study is to predict dioxins emission in peat soil based on the limited emission data and selected physico-chemical properties.

Methodology: An artificial neural network (ANN) was used to predict dioxins concentration in peat soil. The prediction performance of an ANN is affected by uncertainty from its initial weights. Therefore, an optimisation algorithm called differential evolution (DE) is used to optimise the ANN's initial weights and bias to improve the prediction performance. Several ANNs with fixed architecture are used to predict dioxins emission. Each neural network consisted of a multi-layer perceptron with a backpropagation algorithm. Eight input variables and one output variable were adopted to train and test various neural network architectures using real-world datasets. The model optimization procedure was carried out to ascertain the best network architecture in terms of predictive accuracy.

Results: The simulation results showed that the ANN based methodology is a viable alternative which can be performed to predict the dioxins concentration in peat soil.

Conclusion: The prediction model of dioxins emission concentration is applicable as a cost-effective solution for pollution control and environmental monitoring for authorities especially the Fire and Rescue Department to realise actual requirements of operation during fire to avoid dioxins exposure.

KEYWORDS: Dioxins, artificial neural network, peat, prediction modelling, evolutionary algorithm

[DEV-1]
PROCYANIDIN-C1 ALLEVIATES BISPHENOL AF-INDUCED APOPTOSIS, OXIDATIVE STRESS AND MITOCHONDRIAL DAMAGE IN THE EARLY DEVELOPMENTAL STAGES OF ZEBRAFISH EMBRYOS

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ABSTRACT

Introduction: Bisphenol AF (BPAF) is a new bisphenol analogue used in the plastics industry; however, little is known about its potential hazards. BPAF may be consumed by children at higher rates than by adults as a result of inhalation, dermal exposure, and water contact. Procyanidin-C1 (PCY1) has been shown in studies to neutralise free radicals, mitigate the effects of environmental toxins, and protect cells from DNA damage. In this study, the effects of PCY1 on the expression of apoptotic (*baxa, bcl2,* and *casp3a*), mitochondrial (*etfa, mfn2,* and *pink1*), and oxidative stress-related (*gpx1a, nrf1,* and *sod1*) genes in BPAF-exposed zebrafish embryos were determined.

Methods: Zebrafish embryo acute toxicity test (ZFET) was used to evaluate the embryo's toxicity. Toxicological endpoints were monitored every 24 hours until the 96 hours of exposure. Hatching, heart rate, and teratogenicity were all noted as early as 48 hours after conception. Total RNA was isolated, converted to cDNA, preamplified, and processed with a microfluidic quantitative real-time polymerase chain reaction (qRT-PCR). The genes were analysed using BioMark Real-Time PCR Analysis Software.

Results: In BPAF-exposed conditions, PCY1 intervention improves embryonic development by lowering embryonic mortality and malformations. PCY1 intervention significantly reduced the expression of the genes *bcl2* and *casp3a*. The genes *etfa, mfn2, pink1,* and *nrf1* were also significantly down-regulated in this study.

Conclusions: PCY1 has been demonstrated to alleviate BPAF-induced apoptosis, oxidative stress, and mitochondrial damage in early developmental stages of zebrafish embryos. The findings suggest that PCY1 may protect embryos from the deleterious effects of BPAF.

KEYWORDS: Bisphenol AF, procyanidin-C1, apoptosis, oxidative stress, mitochondria

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*blue - physical poster black - virtual

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**blue - physical poster* *black - virtual*

[P1]

TOXICITY EVALUATION OF INHALED IRON OXIIDE NANOPARTICLES WITH DIFFERENT SURFACE CHARGE POLARITIES AGAINST PULMONARY CELLS

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ABSTRACT

Introduction: Metal-based nanomaterial such as iron oxide nanoparticles (IONPs) have received wide attention to be developed for therapeutic applications against lung cancer. However, the toxicity effect of IONPs upon inhalation has not been well studied. This study attempted to evaluate the toxicity mechanism of IONPs with different surface charge polarities in lung cells.

Methodology: PEG-coated-IONPs and amine-coated-IOPNs at various concentrations (0.3 to 1.0 mg/mL) were nebulized onto the air-liquid interface Calu-3 cells using PARI nebulizer for 2 min. Different type of analysis such as measure ATP content, apoptosis, MMP, cytochrome C and caspase were carried out to evaluate the toxicity of IONPs. The cellular uptake elucidation is performed using various endocytosis inhibitors (i.e chlorpromazine, wortmanin etc).

Results: Following the deposition of IONPs via nebulization, the lactate dehydrogenase data showed that the proliferation of Calu-3 was affected with the decreasing trend: positively charged amine-coated-IONPs (proliferation: 35.3 ± 1.2%) < negatively charged PEG-coated-IONPs (56.3 ± 0.6%). In addition, positively charged IONPs were more potent to affect the apoptosis, ATP content, MMP, cytochrome C and caspase 3 levels in Calu-3 cells compared negatively charged IONPs. Both amine-coated IONPs and PEG-coated IONPs were dependent on clathrin-mediated endocytosis for internalization into Calu-3.

Conclusion: Positive charged IONPs was more pronounced in inducing toxicity effect in lung cells compared negative charged IONPs.

KEYWORDS: Surface polarity, inhalation, toxicity, endocytosis, Calu-3

[P2]

IN VITRO TOXICITY STUDIES OF MAGNETIC NANOPARTICLES (MNPS) ON A549 AND MRC5 CELL LINES

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ABSTRACT

Introduction: Magnetic nanoparticles (MNPs) are no strange name in nanoparticles research. MNPs are distinctive with regard to their size, chemical reactivity, energy absorption, and biological mobility. Their superparamagnetic property enables their use as MRI contrast agents, magnetofection agents, artificial hyperthermia agents, and as nanocarriers for targeted drug and gene delivery. Surface coating of MNPs is necessary to prevent nanoparticle agglomeration, oxidation, reduce toxicity and improve their pharmacokinetics and biodistribution. However, there is a scarcity in studies on the toxicological effect of these surface coated MNPs on human.

Method: This work demonstrates the cytotoxicity evaluation of MNP, oleic acid magnetic nanoparticles (MNP-OA), and PEG-coated MNP (MNP-PEG) on both human lung carcinoma (A549) and human lung fibroblast (MRC5). XTT assay were used to investigate the *in vitro* toxicity of the samples. Different concentration of the MNPs (0.2 -1.0 mg/mL) were incubated with the cells for 48 hours in the prepared nanomedia.

Results: All three MNPs showed good biocompatibility in MRC5 cells, with >80% cell viability recorded at the highest concentration of 1.0 mg/mL. However, MNP-PEG showed high toxicity in A549 cells with IC_{50} 0.65 ± 0.07 mg/mL, followed by MNP-OA at 0.76 ± 0.04 mg/mL. Bare MNP maintain non-cytotoxic against A549 cells with > 60% viability even at the highest concentration, IC_{50} 1.72 ± 0.34 mg/mL.

Conclusion: Dose-dependent cytotoxicity trend were observed in A549 cells with decreasing cell viability recorded throughout the increasing concentration of the samples. The ability of MNPs to induce cell death in A549 cells also indicate the potential anticancer properties of the nanoparticles

KEYWORDS: Iron (III) oxide; polyethylene glycol (PEG); oleic acid; cytotoxicity

[P3]

EVALUATION OF ORGANOPHOSPHATE POISONING CASES AMONGST ADULTS RECEIVED BY THE MALAYSIAN NATIONAL POISON CENTRE (2006–2020): A RETROSPECTIVE REVIEW

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ABSTRACT

Introduction: Organophosphate poisoning is a grave public health concern. It is estimated to cause up to three million cases each year resulting in approximately 300,000 causalities and deaths in Asia. This study evaluates poisoning cases amongst adults involving the use of organophosphates based on poisoning exposure calls reported to this centre.

Methodology: Poisoning exposure cases amongst adults aged 20 to 74 years old were retrospectively reviewed from the pesticide poisoning database of the Malaysian National Poison Centre (NPC) from 2006 to 2020.

Results: Within the study period, a total of 6 917 insecticide poisoning cases were recorded. About sixty per cent of these cases were deliberate and were more commonly found amongst male individuals (57%) of the Indian race (36%) aged between 20 to 29 years old (25%), which occurred at home (90%) through the route of ingestion (94%). The largest implicated agent was Chlorpyrifos (20%), followed by Malathion (9%) and other organophosphates (5%). Despite stringent regulations governing the manufacture of insecticides and techniques to reduce the negative impact on people's health, the use of insecticides to commit suicide continues to be a common practice. The extensive use of pesticides in agriculture and the widespread accessibility of obtaining these agents further contribute to this problem.

Conclusion: Results show a significant portion of poisoning committed with suicidal intent and self-harm involves the ingestion of organophosphates. Preventive measures must be undertaken to reduce these incidences from rising.

KEYWORDS: Organophosphates, insecticides, suicidal intent & self-harm poisoning

[P4]

TOXICOVIGILANCE MONITORING IN MALAYSIA THROUGH HAZARD IDENTIFICATION AND RISK CHARACTERIZATION OF TOXIC SUBSTANCES EXPOSURE VIA MyToxData; A POISONING EPIDEMIOLOGY SURVEILLANCE SYSTEM BY THE NATIONAL POISON CENTRE USM

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ABSTRACT

Introduction: Poison centres are key players of toxicovigilance activities since poisoning statistics generated are essential to define the cause, incidence and severity of poisonings occurring in the general population. To date, published epidemiological studies of poisoning cases in Malaysia are minimal and related data are scattered and may not reflect the actual national poisoning burden.

Objectives: This study aims to identify the emergence of new substances as well as trending substances that are frequently implicated in human poisoning exposure cases in Malaysia derived from MyToxData.

Methods: This study used secondary data collected by the NPC, based on call enquiries from healthcare professionals who consult the Drug and Poison Information Service. A retrospective review of the data from 2019 to 2021 recorded in MyToxData system was conducted.

Results: Within the study period of the past three years (2019-2021), the NPC has documented a total of 9077 poisoning cases in MyToxData. During the pandemic, there was a notable surge in the number of poisoning exposure calls from 2020 to 2021. The majority of poisoning exposure calls came from urban areas of the West Coast states; Selangor (21.0%), Perak (18.0%) and Negeri Sembilan (10%). More than half of the exposure was un-intentional (59%) involving more males (55%) as compared with females (43%), within the adult group category (52%). Exposure mostly occurred at home (96%) via oral ingestion (94%). The top three poisoning agents for each year exhibit the same pattern with pharmaceutical products being the highest followed by household products and pesticides. Statistics also show the number of these agents increased more than two-fold in 2020 in comparison to 2019. Emerging poisoning exposures involving adulterated sliming beauty products in the form of candy among children was identified. Whereas for household products, hand sanitizers, cleaning products and laundry detergent pods are also trending.

Conclusion: With changes and evolving trends of poisoning, a relevant, centralised and comprehensive surveillance system is vital. Mytoxdata generates information on evolving trends and identifies toxicovigilance targets so that effective targeted preventive measures and policies can be undertaken to help reduce the national poisoning burden.

KEYWORDS: Surveillance system, poisoning, toxicovigilance, epidemiology

[P5]

POTENTIAL OF BILE PIGMENTS AS INHIBITOR OF CYP2A13 MEDIATED TOBACCO SPECIFIC N-NITROSAMINE METABOLISM: MOLECULAR DOCKING STUDY

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ABSTRACT

Introduction: Tobacco-specific N-nitrosamine, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) are among carcinogenic compounds present in tobacco products including e-cigarettes. Metabolism of NNK by CYP2A13 results in electrophilic species that eventually participate in development of lung cancer. Interaction of bile pigments with CYP and its potential protective roles in cancer have been suggested. This study illustrates the behavior of bile pigments in the CYP2A13 active and allosteric sites using molecular docking approach to study the potential of bile pigments as CYP2A13 inhibitor.

Methods: Molecular docking using AutoDock software was performed to computationally dock the bile pigments and NNK to the active sites of CYP2A13 enzyme and elucidate their interactions with the amino acids of the enzyme. Whereas DoGSiteScorer was used to predict the allosteric sites of CYP2A13 enzyme. The visualization of interactions between the ligands and receptors was carried out using PoseView and PyMOL.

Results: NNK showed consistent binding energies to the active sites of CYP2A13 crystal structures. Bilirubin and biliverdin exhibit lower binding energy to allosteric sites compared to the active site of CYP2A13. The visualization of interactions indicates interactions of bile pigments with amino acids, including the critical residues which is N297.

Conclusion: The study of protein-ligand interactions facilitates exploration and screening of potential inhibitor. From the finding, it can be postulated that bile pigments indicate potential to inhibit the metabolism of NNK by CYP2A13. This finding is valuable as part of an ongoing study to decipher the protective role of bile pigments from the toxicity effect of NNK.

KEYWORDS: Bilirubin, CYP2A13, inhibitor, smoking, tobacco

[P6]

PRENATAL DEVELOPMENTAL TOXICITY STUDY OF MEDICINAL PLANTS IN MALAYSIA: A SCOPING REVIEW FROM 2011 UNTIL 2021

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ABSTRACT

Introduction: Any natural entities cannot be ruled out from toxic effects. Same goes to the medicinal plants. With the escalating numbers of pregnant women using medicinal plants for various purposes, comprehensive prenatal toxicity analysis has to be performed to mitigate any possible harmful outcomes to the developing foetus and pregnant mothers. Therefore, the aim of this review is to summarize the main findings from the prenatal toxicity studies of natural products in Malaysia in the last ten years.

Methodology: Google scholar searched for studies on various natural products for their prenatal toxicity from 2011 to 2021. Eligibility was checked based on selection criteria. Nine articles were included in this review.

Results: There were only eight medicinal plants being assessed for prenatal toxicity. Six of them were reported to exhibit embryo-fetotoxicity retardation effect and incomplete ossification of the skull, sternebrae, and metatarsal bones to foetus.

Conclusion: The use of medicinal plants has received considerable interest. However, a few numbers of plants have been screened for their prenatal developmental toxicity and as evidenced, the majority of them demonstrated toxic effects on foetal development.

KEYWORDS: Prenatal toxicity, natural product, pregnancy, foetus parameters, foetal development.

[P7]
DEVELOPMENTAL TOXICITY STUDY OF *LABISIA PUMILA* VAR. *ALATA* IN RAT WHOLE EMBRYO CULTURE

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ABSTRACT

Introduction: *Labisia pumila* var. *alata* (LPva) has been traditionally used to facilitate childbirth and regain body strength. Although many scientific studies have been conducted, evidence of its toxicity and adverse effects during pregnancy are still limited. This study was conducted to investigate developmental toxicity of LPva extracts using rat whole embryo culture (WEC).

Methods: Rat embryos were collected at embryonic day 10.5 (E10.5) and cultured using continuous aeration WEC system. The conceptuses were cultured for 24 hours (E10.5-E11.5) in 100% immediately-centrifuged rat serum supplemented with 2mg/ml D-glucose. The embryos were exposed to different concentrations of LPva water extracts (10, 50, 100, 500 and 1000 µg/ml) with vehicle as negative control and 5-fluorouracil (0.1, 0.25, 0.5, 1.0 and 8.0 µg/ml) as positive control. Total morphological score (TMS), visceral yolk sac (VYS) diameter, crown rump length (CRL) and head length (HL) were measured.

Results: Growth and development of the conceptuses were significantly different in LPva at 500µg/ml and 1000µg/ml ($p<0.001$) compared to control. TMS of the embryos was decreased in a dose dependent manner with CRL and HL reduced correspondingly. However, no abnormality was recorded. In comparison with 5-fluorouracil, abnormalities were observed in neural tube closure, optic and limb-bud development with TMS, VYS diameter, CRL and HL decreased significantly from 0.5 µg/ml ($p<0.001$). Embryo death was only detected at 8.0 µg/ml.

Conclusion: Findings suggested that LPva extracts may have affected embryonic growth and development which demonstrated toxicity at a higher dose. Further study using a transcriptomic approach may increase the predictivity of developmental toxicity in WEC.

KEYWORDS: WEC, whole embryo culture, *Labisia pumila*, developmental toxicity, embryotoxicity

[P8]

THE OCCURRENCE AND FATE OF SELECTED ANTIBIOTICS IN SEWAGE TREATMENT FACILITIES AND THE EVALUATION OF PHARMACEUTICAL USE IN NORTHERN MALAYSIA BY USING A WASTEWATER BASED EPIDEMIOLOGY APPROACH

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ABSTRACT

Introduction: Despite the rise in antibiotic resistance, Malaysia has never taken an environmental approach to study antibiotic distribution in wastewater. Antibiotics are shed into the environment by the human pharmacokinetic mechanism, with water bodies being the primary site of disposal. Antibiotics in the water, especially wastewater, would thus indicate the emergence of antibiotic resistance. Therefore, thepurpose of this study was to analyse the presence and the fate of four selected antibiotics (Colistin, Polymyxin B, Meropenem, and Vancomycin) in wastewater samples from 18 different sewage treatment plants (STP) in the northern part of Malaysia, paying attention not only to their occurrence andelimination but also to the pharmaceutical usage of these antibiotics in urban populations, by using a wastewater-based epidemiology approach (WBE).

Methodology: For this investigation, solid phase extraction–liquid chromatography-mass spectrometry (SPE–LCMS) was developed and validated to determine the four target antibioticsin wastewater with satisfactory sensitivity (limits of detection below 10 ng/L), accuracy, and precision. The obtained data were then being used to estimate the consumption rate of the population by using the wastewater-based epidemiology approach (WBE).

Result: Antibiotic levels detected were below 1 µg/L with below-average clearance in STPs, with effluent concentrations sometimes greater than influent. Meropenem and Polymyxin B were the most prevalent antibiotics detected, followed by colistin and vancomycin. WBE approach had estimated that Kedah population had consumed up to 55% more antibiotics compared to Penang, despite Penang covered more population compared to Kedah.

Conclusion: Five out of six antibiotics analytes were detected in most wastewater samples and Kedah population was estimated to consume more antibiotics compared to Penang population.

KEYWORDS: Wastewater; bioanalysis; toxicology; wastewater based epidemiology

[P9]
TRIPHENYLTIN(IV) DIISOPROPYLDITHIOCARBAMATE-INDUCES CYTOTOXICITY VIA PARP AND p21 ACTIVATION IN JURKAT T LYMPHOBLASTIC LEUKAEMIA CELLS

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ABSTRACT

Introduction: The antiproliferative effects of five novel di- and triphenyltin(IV) dithiocarbamate compounds represented as R_nSnL_2 (where R=C_4H_9, C_6H_5; n= 2,3; L= *N*,*N*-dithiocarbamate), Ph_2Sn(*N*,*N*-diisopropyldithiocarbamate) (**OC1**), Ph_3Sn(*N*,*N*-diisopropyldithiocarbamate) (**OC2**), Ph_2Sn(*N*,*N*-diallyldithiocarbamate) (**OC3**), Ph_3Sn(*N*,*N*-diallyldithiocarbamate) (**OC4**) and Ph_2Sn(*N*,*N*-diethyldithiocarbamate) (**OC5**) were investigated in Jurkat cells.

Methodology: The cytotoxicity and the mode of cell death were determined via MTT assay and Annexin V-FITC/PI assay, respectively. Cell cycle analysis was conducted to identify the cell cycle arrest. The genotoxicity and the loss of mitochondrial membrane potential were determined via TMRE staining assay and Alkaline Comet assay, respectively. Next, the role of oxidative stress was corroborated via DHE staining assay and NAC assay. The caspase cascade activation was further determined via caspase-9, -8 and -3 activation assay. Finally, western blot analysis was conducted to rationalize the cytotoxicity-associated protein expressions.

Results: All compounds produced potent cytotoxicity with low IC_{50} values (0.1 µM – 7.1 µM) and induced about 55-86% apoptotic events. **OC2** showed the strongest effect by displaying the highest selectivity index (SI > 2) against Jurkat cells, hence, was selected for further studies. **OC2** induced apoptosis via intrinsic apoptosis pathway by modulating mitochondrial membrane perturbation which was triggered by DNA damage and subsequently, produced excessive ROS as well as cleaved-PARP. The role of oxidative stress was confirmed through the significantly reduction of apoptosis percentage in NAC-pretreated cells. Moreover, **OC2** arrested the cells' progression in the G_0/G_1 phase via the activation of p21.

Conclusion: OC2 has a potentially beneficial effect on antileukaemic properties by inducing mitochondrial-mediated apoptosis and cell cycle arrest.

KEYWORDS: organotin, apoptosis, genotoxicity, molecular mechanism, cell cycle

[P10]

THE CYTOTOXICITY EVALUATION OF VARIOUS NANOPARTICLES TOWARDS *Artemia salina* CYST

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ABSTRACT

Introduction: Nanoparticles (NPs) are currently used in a wide variety of commercial applications and disciplines, including technology, industry, and medicine. As a result of the manufacture, distribution, application, and disposal of associated NPs, they are unavoidably released into aquatic ecosystems, particularly marine ecosystems. Aquatic creatures are largely vulnerable to the harmful effects of NPs due to their direct or indirect effects. This work demonstrated the biocompatibility of various NPs with *Artemia salina* (*AS*) cysts by exposing a variety of NPs, including iron oxide (IO), graphene oxide (GO), reduced graphene oxide (RGO), zinc oxide (ZnO), and titanium dioxide (TiO_2).

Methodology: The *AS* cyst is incubated for 24 to 48 hours using salt water treated with NPs using different concentration. Finally the hatching rate were determine.

Results: The *AS* exposed to IO showed no slight effect on the hatching rate. Cysts may be less susceptible to IO NPs due to their cortical membrane, which acts as a protective shield against the IO. Next is GO; when it is in a higher concentration, the hatching rate drops significantly. At a concentration of more than 0.5 mg/mL, few cysts hatched due to the sharp edge of the GO, which had torn the cyst capsule. When *AS* is exposed to TiO_2 at a concentration of up to 0.25 mg/mL, the hatching rate increases slightly. Thus, it is confirmed that at low concentrations, TiO_2 increased the hatching rate. The hatching rate decreased from 0.5 mg/ml onward. The hatching rate of *AS* was less than 10% when it was exposed to ZnO. This could be explained by the high level of oxidative stress caused by Zn ions.

Conclusion: In conclusion, shape and particle size cannot be the sole determinants of cyst hatching percentage. IO and TiO_2 are biocompatible with the *AS* cyst. The ZnO and GO have a low hatching rate of *AS* cysts.

KEYWORDS: *Artemia salina*; iron (III) oxide; graphene oxide; reduced graphene oxide; titanium dioxide; zinc oxide

[P11]
ECOTOXICITY TO SALTWATER ORGANISM AND CYTOTOXICITY OF BIOGENIC SYNTHESIS OF REDUCED GRAPHENE OXIDE-SILVER NANOCOMPOSITE

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ABSTRACT

Introduction: Nanocomposites incorporating carbon and metal nanoparticles would greatly improve biological applications due to their unique physiochemical features, large surface area, and potent inhibitory action. The aim of the present study was to investigate the eco-cytotoxicity of biogenic reduced graphene oxide-silver nanocomposite (rGO-Ag) in comparison to reduced graphene oxide (rGO) and silver nanoparticles (AgNPs) using leaf extract of *Clinacanthus nutans*.

Methodology: The eco-toxicity was conducted towards brine shrimp aquatic species (*Artemia salina*) cysts and on human adenocarcinoma cell lines (lung cell line, A549 and colorectal cell line, Caco2) using XTT assay. The eco-toxicity was done by monitoring the hatching of the cysts. In a 96 well plate, 10 cysts were placed in each well. Then, each well was filled with 200 µL of solution at various concentrations. The plates were incubated under continuous illumination at a temperature of 28 °C. Using a microscope, the number of hatched cysts exposed to nanocomposite were determined. For the XTT assay, approximately, 4 x10^3 cells were seeded in 96 well plates and were incubated for 48 h at 37 °C in a CO_2 incubator with different concentration of rGO-Ag nanocomposite (control, 0.5, 1.0, 5.0, 10.0, and 25.0 µg/mL). To determine the cell viability, XTT dye was added to each well and incubated for 4 h at 37 °C in a CO_2 incubator. Optical density was measured using a microplate spectrophotometer at wavelength of 450 nm absorbance.

Results: For the ecotoxicity hatching assay of *Artemia salina* cysts demonstrated AgNPs and rGO-Ag nanocomposite showed a dose-dependent decrease in the hatching rates, however, rGO showed higher hatching rate in the selected concentration range of 0.001 to 1.0 mg/mL. The *in vitro* study revealed that rGO has low cytotoxicity against A549 and Caco2 cell lines. However, AgNPs and rGO-Ag nanocomposite demonstrated dose-dependent cytotoxicity effect towards both A549 and Caco2 adenocarcinoma cell lines.

Conclusion: The present study provides evidence of the potential risks of rGO-Ag nanocomposite again aquatic organism and their effect on public health.

KEYWORDS: Biogenic; cytotoxicity; cell lines; ecotoxicity; reduced graphene oxide-silver nanocomposite

[P12]

AXL: A POTENTIAL TARGET TO ALLEVIATE TETRACYCLINE INDUCED LIVER STEATOSIS

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ABSTRACT

Introduction: Drug-induced steatosis is one of the major toxicological challenges for usage of Tetracycline, Methotrexate, Valproic Acid etc. It is known to be exacerbated with a high fat diet. Thus, it is important to identify cellular targets to alleviate drug-induced steatosis. Axl, a member of TAM receptor tyrosine kinase (RTK) family and is known to be upregulated in development of liver fibrosis. Thus, we were interested in understanding the role of AXL in the development of drug-induced steatosis.

Methods: In this study we treated HepG2 cells with oleic acid and Tetracycline to induce steatosis. Further, we used pharmacological inhibitors of AXL, such as Bemcentinib to understand the role of AXL in the development of steatosis. Changes in lipid accumulation was observed by measuring intensity of lipid binding dye, BODIPY (493/503) using flow cytometer. Further, we used RT-PCR and western blot techniques to observe mRNA and protein level changes in genes involved in lipid metabolism.

Results: It was observed that tetracycline induced *de novo* lipogenesis as well as lipid uptake by inducing expression of corresponding genes such as SREBP1c and CD36 respectively. However, AXL inhibition down regulated expression of SREBP1c by 10 folds while CD36 was reduced by approximately 4 folds. Moreover, AXL inhibition upregulated PPARα and CPT1 significantly to increase β-oxidation.

Conclusion: These results identify AXL inhibition as a promising strategy to control Tetracycline induced steatosis and avoid further toxicity issues.

KEYWORDS: Drug-induced steatosis, AXL, tetracycline-induced steatosis, receptor tyrosine kinases, lipid metabolism

[P13]

RETROSPECTIVE STUDY: *IN VITRO* CYTOTOXICITY TESTING TOWARDS DIFFERENT MEDICAL GLOVES MATERIALS

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ABSTRACT

Introduction: Biocompatibility testing of medical devices is used to evaluate their safety prior to usage in a clinical setting. *In vitro* cytotoxicity testing is one of the essential biocompatibility testing which utilize the use of tissue cells as the host system to determine the biocompatibility of the medical devices or the materials they are composed from with the host system, and its potential toxicity effects towards the cell. It is a required endpoint for all types of medical devices which includes the medical gloves.

Methodology: This retrospective study evaluates the cytotoxicity effect of different medical gloves materials based on qualitative *in vitro* cytotoxicity testing performed according to ISO 10993 guidelines, specifically using the extraction method. L-929 mouse fibroblast cells were seeded into a 24-well plate and morphological changes of the cell were observed before and after exposure of the medical gloves extract towards the cells and were graded according to the guidelines to determine the cytotoxic effect due to medical devices extract. Data of the *in vitro* cytotoxicity testing conducted throughout the year 2020 to 2021 towards 33 pairs of medical gloves from different manufacturers were collected .

Results: Out of all 33 samples, 60.6% (n=20) of them were made up of nitrile rubber, 36.4% (n=12) were made up of latex rubber and 3.0% (n=1) was made up of polychloroprene rubber. Results revealed that severe reactivity responses (grade 4) were observed in morphological evaluation of the cells exposed to 100% extract of the medical gloves in all three different type of materials, where nearly complete or complete destruction of the cell layers were observed. Only one pair of gloves made up of nitrile rubber demonstrated moderate reactivity (grade 3) at 100% concentration of the medical glove extract.

Conclusion: This study suggests that medical gloves made up of these three materials possess cytotoxic effects and may explain the severe allergic reactions associated with prolonged and frequent usage of these types of medical gloves. Thus, consideration shall be taken in choosing the medical gloves materials and any medical devices product that involves direct contact with the skin.

KEYWORDS: Cytotoxicity testing, medical gloves, biocompatibility, *in vitro*, medical devices

[P14]

ADVERSE DRUG REACTION CHARACTERISTICS TO N-ACETYLCYSTEINE FOR ACETAMINOPHEN OVERDOSE IN A TERTIARY INSTITUTION IN SINGAPORE

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ABSTRACT

Introduction: Acetaminophen is the most common pharmaceutical medication involved in poisoning in Singapore. While N-acetylcysteine is a beneficial antidote for the management of acetaminophen overdose, N-acetylcysteine is associated with a high risk of adverse effects and anaphylactoid reactions.

Methodology: A retrospective review of acetaminophen poisoning cases presenting to Singapore General Hospital from January 2018 to September 2021 was conducted. Cases were identified by retrieving the records of all patients who had N-acetylcysteine administered and serum acetaminophen levels performed during this time period. Electronic medical records were subsequently reviewed to retrieve demographic data and details on case presentation.

Results: A total of 124 cases of acetaminophen overdose necessitating treatment with N-acetylcysteine were identified. 24 patients (19.4%) developed adverse reactions to N-acetylcysteine. Adverse drug reactions developed at a mean time lag of 71.0 minutes from the start of administration. Reactions occurred mostly during administration of the loading dose (54.2%; n=13). All patients had skin manifestations (flushing, pruritus or urticaria). Only three patients (2.4% of all N-acetylcysteine cases) presented with respiratory symptoms of adverse drug reactions (one with breathlessness, one with breathlessness and cough, and one with rhonchi). Two cases (1.6% of all N-acetylcysteine cases) had otherwise severe reactions causing cardiorespiratory compromise. None required mechanical ventilation or admission to intensive care.

Conclusion: Although N-acetylcysteine is an effective antidote for acetaminophen overdose, the high incidence of adverse drug reactions and anaphylactoid reactions associated with the traditional three-bag dosing regimen warrant consideration for the adoption of other dosing regimens with superior side effect profiles instead.

KEYWORDS: Paracetamol; acetaminophen; N-acetylcysteine; adverse drug reaction; anaphylactoid

[P15]

BIOCOMPATIBILITY ASSESSMENT OF ColPatch™ AS AN IMPLANTABLE MEDICAL DEVICE IN WOUND CARE MANAGEMENT

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ABSTRACT

Introduction: Collagen is an important and abundant protein, accounting for ~25% of total protein in the human body. Exogenous collagen type I (col) is an authentic alternative approach in the medical, pharmaceutical and food industries, nowadays. In addition, collagen-based materials have been used for a range of biomedical applications including implantable medical devices for tissue regeneration.

Methodology: Collagen from ovine (*Ovies aries*) was extracted according to the procedure established by Fauzi et al. 2016 under sterilised conditions. The final concentration of 14 mg/ml was achieved by dissolved in 0.35 M (v/v) acetic acid overnight at 4°C and poured into the well plate and pre-frozen at −80°C for 6hr followed by the -40.0 to -49.5°C and 0.4 – 0.5 mBar pressure of freeze-drying method (Ilshin, Korea) for 24–48 hours. The final products were tested for toxicity testing based on ISO 10993-5, ISO 10993-10, ISO 10993-11, USP 40.2017<151> and OECD 471.

Result: Grade 0 (non-reactive) based on ISO 10993-5:2009 was graded for the sample at 100% concentration and the mean number of the revertant colonies of ColPatch™ did not exceed 2-fold of the 0.9% w/v sodium chloride compared to the tester strain *S. typhimurium (TA100,TA1535, TA98, TA1537* and *E.coli WP2* trp uvrA. For the dermal sensitization assay, none of 10 male guinea pigs used in this study displayed any erythema or edema effect ($p>0.005$). The sample extraction was injected into 5 female mice and demonstrated no significant difference in mortality rate and weight body changes compared to 0.9% normal saline after 3-days of observation. Besides, no abnormalities were detected in the clinical observation and necropsy findings.

Conclusion: This biocompatibility assessment unraveled ColPatch™ has no adverse effect in respective studies of induced skin sensitization effect, mutagenic and cytotoxic. Therefore, ColPatch™ is a potential medical device candidate for future wound management.

KEYWORDS: COL-I, biocompatibility, ovine tendon collagen

[P16]
HYDROGEN SULPHIDE AMELIORATES THE TOXIC EFFECT OF CLOTRIMAZOLE AGAINST TRICHOPHYTON RUBRUM

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ABSTRACT

Introduction: Reactive sulphur species (RSS), including hydrogen sulphide anion has been recently discovered to be a part of a major endogenous antioxidant system. Nonetheless, the RSS was implicated as an underlying mechanism in reducing the efficacy of several antibiotics such as penicillin. The emergence of drug resistance has been a global concern. In fact, several incidences on the azole resistant Trichophyton isolates in the clinical setting such as clotrimazole have also been reported. Clotrimazole is a broad-spectrum antifungal commonly used in the management of dermatophytosis management. Dermatophytosis can be caused by *Trichophyton* families including *Trichophyton rubrum.* This study investigated the role of RSS, particularly hydrogen sulphide as a potential element underlying the resistance against clotrimazole.

Methodology: The *T. rubrum* growth in sulphide-rich environment was initially measured by culturing the subject in media supplemented with several concentrations of sodium hydrosulphide (NaHS). Then, the subjects were treated with 1000 µM of clotrimazole, with or without co-treatment with several concentrations of NaHS. Minimum inhibitory concentration (MIC) test was performed to observe the growth of the subjects.

Results: Clotrimazole significantly reduced the growth of *T. rubrum*. Interestingly, the subjects exhibited increase gradual survivability when co-treatment with higher concentrations of NaHS was performed in a dose-dependent manner.

Conclusion: Endogenous RSS potentially interferes with the efficacy of clotrimazole. The exact mechanism underlying such activity warrants further investigation. Whether the interaction shown in this study is observable in other types of RSS-donours or antifungal agents will be interesting to be investigated.

KEYWORDS: **Dermatophytes, *Trichophyton rubrum*, antifungal resistance, clotrimazole, reactive sulphur species (RSS)**

[P17]
SUBACUTE TOXICITY OF MICROGRANULATED *Myrmecodia platytyrea* AQUEOUS TUBER EXTRACT (gMPAE)

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ABSTRACT

Introduction: *Myrmecodia platytyrea* or locally known as 'Sarang Semut' is an epiphytic plant native to Asia and the Asia Pacific regions. The tubers of this plant were traditionally used in the management of cancer, hyperuricemia and coronary heart diseases. Scientifically, it has been proven that the aqueous extract of this tuber has potential pharmacological benefits including anti-cancer, anti-diabetic and anti-inflammatory properties, to name a few. Hence, the extract has the potential to be developed as a supplement in boosting the immune system since the extract showed no acute and subacute toxic effects. The aim of this study is to investigate the subacute toxicity of the microgranulated aqueous extract of *M. platytyrea* tuber (gMPAE).

Methodology: The subacute toxicity study was carried out based on the OECD guidelines 407. The female nulliparous and non-pregnant ICR mice were divided into three groups (n=5), consisting of a group treated with normal saline (control group), a group treated with a placebo (microgranules), and a group treated with gMPAE. The mice were given the treatments orally once daily for 28 days.

Results: The findings showed no physical or behavioral changes in both placebo or gMPAE treated mice compared to the control mice. No mortality was also observed after 28 days of administration. The mice also showed no signs of delayed occurrence of toxic effects, 14 days post-treatment.

Conclusion: gMPAE, a newly formulated aqueous extract demonstrated no toxic effect after 28 days of daily oral treatment thus safe for consumption.

KEYWORDS: ***Myrmecodia platytyrea*; microgranules; subacute toxicity; immune response; anti-inflammatory**

[P18]

ACUTE TOXICITY ASSESSMENT AND BEHAVIOURAL RESPONSE OF CURCUMIN DERIVATIVE, BDMC33 IN ZEBRAFISH (*Danio rerio*) LARVAE

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ABSTRACT

Introduction: Acute toxicity test is the first step in any pharmacological screening procedure to determine the safety dose, before evaluating drug effects on the human body. BDMC33 2,6-bis (2,5-dimethoxylbenzylidene) cyclohexanone, an analogue of curcumin, is a newly synthesized compound with potential anti-inflammatory effects. Therefore, in this study, we investigated the effect of BDMC33 on acute toxicity and behavioural response in zebrafish larvae before evaluating its efficacy as an anti-inflammatory drug candidate.

Methodology: At first, zebrafish (AB) embryos were exposed to BDMC33 at seven concentrations (2.5-50 µM). Then, the effect of BDMC33 on zebrafish embryogenesis (24-120 hpf) and cardiotoxicity (96 hpf) were observed using the Danioscope. Finally, the behaviour parameter (distance moved) was recorded using DanioVision at 120 hpf. Untreated larvae were used as negative control.

Results: Zebrafish embryos treated with BDMC33 were survived (>50%) at concentration <6.25 µM. The LC_{50} of BDMC33 towards the zebrafish embryo at 120 hpf was 6.25 µM. Zebrafish larvae at 96 hpf showed normal heartbeat upon BDMC33 (2.5, 12.5 and 50 µM) treatment with average value of 119 beats/mins. Normal embryogenesis was observed at <6.25 µM of BDMC33, whereas teratogenic effects were found at the highest concentration tested of 50 µM, which showed spine curvature, bend tail and pericardial oedema. Average distance travelled larvae exposed with BDMC33 was significantly reduced at the highest concentration of 50 µM (159.34±12 mm) compared to untreated larvae (243.09±22 mm).

Conclusion: Our preliminary *in vivo* assessment on acute toxicity and behaviour response of zebrafish exhibits that BDMC33 has low toxic effects at concentration <6.25 µM and could be a potential drug candidate to treat inflammatory diseases.

KEYWORDS: Acute toxicity, BDMC33, behavioural response, LC_{50}, zebrafish

[P19]

GROWTH INHIBITION EFFECT OF SF1 FROM *Clinacanthus nutans* LEAVES ON MICE XENOGRAFT MODEL FOR HUMAN CERVICAL CANCER

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ABSTRACT

Introduction : Cervical cancer is one of the major cause of deaths among women. The current anticancer drugs remain inefficient due to lack of specificity to inhibit the growth of cancer cells. Our old folks believed that medicinal plants improve survivorship. This study aimed to determine the inhibition of tumor growth that is responsible for the anticancer mechanism of standardized fraction, SF1 from *Clinacanthus nutans* as a potential alternative treatment for cervical cancer.

Methodology : SF1 was isolated from a series of bioassay-guided fractionation of *C. nutans* leaves. Female nude mice were used as a tumor model and were xenografted with human cervical cancer, SiHa cells, subcutaneously. When the tumor volume reached 100 mm^3, SF1 was intraperitoneally injected once daily for 28 days. Tumor and liver were fixed for hematoxylin and eosin (H&E) staining and immunohistochemistry (IHC) using caspase-3. Blood was collected by cardiac puncture for assessment of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels.

Results : SF1 showed tumor inhibition rate with more than 50% of tumor growth was retarded compared to the negative control (0.0l% DMSO) group. ALT and AST levels in SF1-treated mice remained in normal ranges compared to the positive control group, cisplatin indicating no sign of toxicity. The H&E analysis of SF1-treated group revealed no indication of liver toxicity and the number of tumor mitosis was reduced. Caspase-3, a critical mediator of apoptosis was shown to be overexpressed in the IHC analysis of SF1-treated group.

Conclusion : SF1 demonstrated anticancer activity by inhibiting the growth of tumor cells via apoptosis pathway.

KEYWORDS: *Clinacanthus nutans*, standardized fraction, anticancer, xenograft, apoptosis

[P20]

CHEMOPREVENTION STRATEGY VIA POLYAMINES PATHWAY INDUCED BY *Clinacanthus nutans* AND *Piper sarmentosum* IN HUMAN LUNG ADENOCARCINOMA CELLS, A549

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ABSTRACT

Introduction: Polyamine is a group of aliphatic amines that necessary for cell growth and development. However, potential of developing a cancer enhanced with the increase of polyamine levels in the body. Since polyamines can be obtained through diet intake, it is essential for cancer patients to consume foods that have low level of polyamines. Therefore, this study aimed to determine the polyamine level of selected plant, Sabah Snake Grass (*Clinacanthus nutans*) and Daun Kadok (*Piper sarmentosum*).

Methods: The antiproliferative effect of *C. nutans* and *P. sarmentosum* were investigated using MTT assay and trypan blue exclusion assay in human lung carcinoma cells, A549. Protein contents were determined based on Lowry assay. The polyamines content in these plants and intracellular content were quantified using High Performance Liquid Chromatography (HPLC). The gene expression analysis was done using qPCR.

Results: The results showed that polyamines content in *C. nutans* (41.49 nmol/g) and *P. sarmentosum* (55.01 nmol/g) are classified under low level. The IC_{50} values for *C.nutans* and *P.sarmentosum* were 10 mg/ ml and 15 mg/ ml, respectively. It has been demonstrated that both plants inhibit the A549 cell's growth after 24- to 96-hours of exposure. Depletion of intracellular polyamine after 24 hours to 96 hours of exposure also identified.

Conclusion: *C. nutans* and *P. sarmentosum* have potential as chemopreventive herbs since they demonstrated capabilities to reduce cell proliferation and decrease in PA and protein content in cells. Further investigation is warranted to evaluate the mode of cell death and the effect on normal cells.

KEYWORDS: Polyamines, natural product, ODC, SSAT

[P21]

CYTOTOXICITY OF *Garcinia mangostana* AQUEOUS EXTRACT ON HepG2 LIVER CANCER CELL LINE

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ABSTRACT

Introduction: *Garcinia mangostana* or commonly known as mangosteen belongs to the family of Clusiaceae which are native to Southeast Asia. Studies have shown that extract of the pericarp of mangosteen contained phytochemicals that exhibit anticancer effects on several cancer cell lines. In the present study, we investigated the cytotoxic effect of aqueous extract of mangosteen against human hepatocellular carcinoma (HepG2) cells.

Methods: The cytotoxicity activity of the *Garcinia mangostana* aqueous extract was conducted at concentrations of 25, 50, 100, 250, 500, 750, and 1000 µg/mL in HepG2 cells upon 24 hours treatment using 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide (MTT) assay. This study was performed in triplicate, and the average values were calculated. IC_{50} was determined from the dose response curve.

Results: *Garcinia mangostana* aqueous extract showed IC_{50} value of 743 µg/mL, in which indicated weak cytotoxic activity on HepG2 liver cancer cell line. The cell viability decreased in a dose-dependent manner started at the concentration of 250 µg/mL.

Conclusion: This finding suggested that aqueous extract of *Garcinia mangostana* exhibited high IC_{50} value which showed that it is a weak chemotherapeutic agent against liver cancer cell. Nevertheless, other types of extracts and cancer cell lines need to be further investigated to confirm its anticancer potential.

KEYWORDS: Mangosteen; hepatocellular carcinoma; cytotoxicity; MTT assay; natural product toxicology

[P22]

IN VITRO MUTAGENIC ACTIVITY OF *Hibiscus sabdariffa* BASED PRODUCT

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ABSTRACT

Introduction: *Hibiscus sabdariffa* has been utilised as food, drink, and herbal medicine in human. However, there is still limited data of its mutagenicity study. Therefore, *in vitro* Ames test was performed to investigate *Hibiscus sabdariffa* based product (HSBP) mutagenic activity using Muta-ChromoPlate™ Assay Kit. In drug discovery and development, the Ames test is one of the requirements in genotoxicity studies prior to human clinical trials.

Methods: The HSBP was prepared in sterile water and filtered using 0.22 µm membrane filter before use. The mutagenicity test was conducted using 96-well microplate. Five different concentrations (0.25, 0.5, 1.0, 2.0 and 5.0 mg/ml) of HSBP were evaluated using two *S. typhimurium* strains, TA98 and TA100.

Results: In our preliminary results, significant mutagenic activity of HSBP in TA98 strain without the metabolic activation was observed starting at the concentration of 0.5 mg/ml whereas the activity in TA100 strain with metabolic activation demonstrated signs of mutagenicity at a higher concentration, 1.0 mg/ml and above.

Conclusion: Based on these findings, HSBP was observed to have mutagenic activity with base-pair mutation in the absence of S9 metabolic activation and possibly frameshift mutation in the presence of metabolic activation. Further studies using other strains are required including *S. typhimurium* TA97a, TA1535, and *E. coli* WP2 uvrA to obtain a thorough safety profile and conclusive genotoxic risks of HSBP.

KEYWORDS: *Hibiscus sabdariffa*; mutagenicity; Ames test; bacterial reverse mutation assay; Muta-ChromoPlate™

[P23]

IN VITRO TOXICITY ASSESSMENT OF *Swietenia macrophylla*

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ABSTRACT

Introduction: The seed of *Swietenia macrophylla* from the family Meliaceae is used as a traditional medicine. Several cases of liver injury were reported in 2018, suspected to be associated with *S. marcrophylla* seed consumption. Previously, we found that the 50:50 water:ethanol, 100% ethanol, and 100% methanol extracts only decreased approximately 50% of HepG2 cell viability based on 3, (4, 5-dimethylthiazolyl-2)-2, 5-diphenyltetrazolium bromide (MTT) assay, after 24 hours exposure at 1000 µg/ml. Increasing the exposure time to 48- and 72-hour did not further decrease the viability. In this study, *S. macrophylla* seed was extracted successively with hexane, chloroform, ethyl acetate, methanol, and water to obtain all the possible non-polar and polar constituents for *in vitro* toxicity assessment.

Methodology: The hexane, chloroform, ethyl acetate, methanol, and water fractions of *S. macrophylla* seed were subjected to cytotoxicity evaluation using HepG2 cell line as an *in vitro* liver model and the MTT assay to measure cell viability. Cells were exposed to each fraction for 24 hours.

Results: Based on the dose-response curves and the value of the 50% inhibitory concentrations (IC_{50}), the hexane, chloroform, and ethyl acetate fractions were more cytotoxic (IC_{50} 615 ± 96, 146 ± 26, and 308 ± 153 µg/ml, respectively) than the methanol fraction (IC_{50} ≥ 1000 µg/ml) towards HepG2 cells. On the other hand, the water fraction showed cell proliferation.

Conclusions: This study indicates that *S. macrophylla* seed contains cytotoxic constituents in the order of chloroform > ethyl acetate > hexane > methanol fractions while addition of the water fraction results in HepG2 cell proliferation. Our next objective is to investigate how *S. macrophylla* affects the glycolysis and tricarboxylic acid (TCA) cycle pathways to impact energy generation and cell viability.

KEYWORDS: *Swietenia macrophylla*, cytotoxicity, *in vitro* toxicity, MTT assay

[P24]

ACUTE TOXICITY EVALUATION OF *CINNAMOMUM VERUM*, *GARCINIA ATROVIRIDIS* AND *VERNONIA AMYGDALINA* DELILE LEAVES

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ABSTRACT

Introduction: Medicinal plants are widely regarded as safe and possess various traditional claims. However, many of these claims have not been scientifically proven. Establishing scientific evidence is crucial to promote medicinal plants' effectiveness and safety. In this study, we investigated the acute toxicity effect of *Cinnamomum verum* (Kayu Manis; CV), *Garcinia atroviridis* (Asam gelugor; GA) and *Vernonia amygdalina* Delile (Bismillah; VA) in vivo.

Methodology: Female Sprague Dawley rats were orally administered with a single dose of aqueous extract of the plants following the OECD Guideline for Testing of Chemicals, no. 420. Dose levels of 300 mg/kg and 2000 mg/kg were used during the sighting study (n=1/dose level/plant). In the main study, 2000 mg/kg was administered (n=4/plant). Animals were monitored for 14 days prior to necropsy.

Results: An increase in body weight was seen in all animals on day 7 & 14. Neither mortality nor toxicity signs were observed during the study. Food intake was normal. Gross pathological assessment during necropsy revealed reddening of ileum (n=2 for CV and GA, n=1 for VA), bilateral enlargement of uterine horns with prominent blood vessel (n=1 for GA) and blunted edge of liver (n=1 for GA).

Conclusion: Microscopic examination of the organs showing abnormality is needed to postulate whether the pathological changes are treatment-related. As the highest dose used in the study did not cause death, the median lethal dose (LD_{50}) of CV, GA and VA is suggested to be >2000 mg/kg BW. Further repeated dose study would be beneficial to determine the effect of prolonged consumption.

KEYWORDS: Toxicity, in vivo, *Cinnamomum verum*, *Garcinia atroviridis*, *Vernonia amygdalina*

[P25]

ACUTE ORAL TOXICITY STUDY OF *Tamarindus indica* AND *Labisia pumila* ON SPRAGUE DAWLEY RATS

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ABSTRACT

Introduction: The fruit pulp extract of *Tamarindus indica* (TI) has been reported for its antioxidant and hypolipidemic properties. Meanwhile, *Labisia pumila* (LP) is traditionally used to maintain healthy female reproductive function and as postpartum medicine. The study aims to evaluate the potential acute oral toxicity of *Tamarindus indica* (TI) fruit extract, *Labisia pumila* leaf (LPA) and root (LPR) extract in single dose oral administration in Sprague Dawley rats.

Methodology: This study was conducted in accordance with test guideline 420 under the Organisation for Economic Co-operation and Development (OECD). After administration on the first day, the rats were observed for morbidity and mortality twice daily and general clinical observations once daily for 14 days. Then, on day 15, the rats were necropsied.

Results: Body weight of the test system increased weekly for all extracts except for LPR-2000 mg/kg group (n=2) which body weight decreased 2.95% and 5.36% on the second week of the study. Macroscopic evaluation on the organs of test system showed reddening of ileum with prominent Peyer's patches for TI-2000 mg/kg group (n=1), LPR-2000 mg/kg group (n=1) and TI-300 mg/kg (n=1) group. Blunt edges at caudal part of spleen were detected (n=2) in TI-2000 mg/kg group. Dilated uterine horns in LPA-2000 mg/kg group (n=2) and generalized uneven surface of the lung parenchyma with soft consistency in LPA-300 mg/kg group (n=1) was observe in each respective treated group. LPR-2000 mg/kg group showed left lateral lobe nutmeg liver (n=1) and generalized pallor of right cranial lobe of the lung (n=1).

Conclusion: The LD_{50} value for TI and both extracts for LP are estimated to be greater than 2000 mg/kg of body weight since there were no mortality and toxicity effect. The gross changes should be further confirmed microscopically.

KEYWORDS: Acute toxicity; *Tamarindus indica; Labisia pumila* aerial*; Labisia pumila* root*; Sprague Dawley*

[P26]
ACUTE AND SUB-ACUTE ORAL TOXICITY OF *Baeckea frutescens* HEXANE EXTRACT IN RATS

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ABSTRACT

Introduction: *Baeckea frutescens (B.frutescens)* of the family Myrtaceae has been used in traditional medicine and was scientifically proven to possess various properties such as antibacterial, antioxidant, anti-inflammatory and anticancer. The study aims to determine the acute and subacute toxicity of hexane extract of *B.frutescens* hexane leaves extract in Wistar rats.

Methods: The acute and subacute toxicity tests were performed according to the OECD guidelines. In the acute oral toxicity test, Wistar rats were administered by oral gavage with a single limit dose of 2000 mg/kg of *B.frutescens* hexane leaves extract. Body weight and toxic signs were monitored twice daily for 14 days. In the subacute oral toxicity test, *B.frutescens* hexane leaves extract were administered by oral gavage to both female and male rats at 100, 200 and 400 mg/kg body weight daily up to 28 days. Blood samples were collected to measure biochemical and haematological parameters whilst gross and microscopic pathology analysis were performed to the kidney and liver samples.

Results: In acute oral toxicity, no dose-related mortality or toxic signs were observed. This suggests the LD_{50} of *B.frutescens* hexane leaves extract is greater than 2000 mg/kg bodyweight. In the subacute toxicity study, rats treated with *B.frutescens* hexane leaves extract did not show any changes in food consumption, body weight, biochemical and haematological parameters compared to the control group. In the histopathological examination, no significant alteration was observed in the liver and kidney of the treated rats.

Conclusions: The LD_{50} of *B.frutescens* hexane leaves extract is greater than 2000 mg/kg bodyweight with no toxicity signs. The findings from this study concludes tolerability of *B.frutescens* hexane extract administered daily for 28 days is up to 400 mg/kg. The extract does not produce any toxic effects in rats after acute and sub-acute treatments.

KEYWORDS: *Baeckea frutescens,* hexane extract, acute toxicity, subacute toxicity, rodents