MONASH University

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MALAYSIAN SOCIETY OF PHARMACOLOGY AND PHYSIOLOGY (MSPP)

Trailblazing The Translational Research | 15 - 17 July 2021 • Virtual Meeting

Malaysian Society of Pharmacology & Physiology (MSPP)

34th Scientific Meeting 2021

frontiers Event Abstracts

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Welcome to the 34th MSPP Scientific Meeting 2021

The Malaysian Society of Pharmacology and Physiology (MSPP) has been the primary Malaysia learned society of pharmacologists and physiologists for more than 33 years. The Society has been organizing its own Scientific Meetings as a platform for researchers to share their research findings and build networking and collaborations. To date, MSPP is proud to have organized 34 scientific meetings. Due to the pandemic, for the first time the 34th Scientific Meeting of MSPP was held virtually on July 15-17, 2021. The meeting which was organized by Monash University Malaysia together with MSPP in collaboration with several local and private universities in Malaysia had attracted 700 delegates from locally and abroad and received more than 160 abstracts. The scientific programme this year focused on translational research under the theme 'Trailblazing the Translational Research'. The three-day conference provided opportunities for sharing and exchanging evidence-based practices and scientific endeavors among physiologists, pharmacologists, physicians, general practitioners, scientists and allied health professionals.

LIST OF ORGANIZERS

Jeffrey Cheah School of Medicine and Health Science, Monash University Malaysia
Malaysian Society of Pharmacology and Physiology (MSPP)

34th MSPP 2021 Programme
"Trailblazing the Translational Research"

Day 1: 15th July 2021

Programme

8.30 am – 9.15 am	**Opening Ceremony** **Speakers** *Prof. Dr. Nafeeza Hj Mohd Ismail* *(President, MSPP; International Medical University)* *Prof. Dr. Shajahan Yasin* *(Head, JCSMHS, Monash University Malaysia)* *Assoc. Prof. Dr. Mohd. Farooq Shaikh* *(Chair, 34th MSPP 2021; Monash University Malaysia)*
9.15 am – 10.00 am	**Keynote Address** *Prof. Dr. Gordon Harold Williams* *Professor of Medicine, Harvard Medical School, USA* **Title: Personalized Medicine: The Link Between People, Animals and Cells**
10.00 am – 10.30 am	**Break**
10.30 am – 11.00 am	**Plenary Lecture 1** *Prof. Dr. Wayne Hodgson* *Monash University, Australia* **Title: Things That Bite and Sting: The Pharmacological Characterization of Animal Venoms and Toxins**
11.00 am – 12.00 pm	**Sponsored Seminar** *Labquip Sdn. Bhd*

12.00 pm – 2.00 pm	Lunch Break
2.00 pm – 3.00 pm	MSPP Young Investigator Award 2021
3.00 pm – 3.30 pm	Break
3.30 pm – 5.30 pm	MSPP Annual General Meeting
Day 2: 16th July 2021	
9.00 am– 9.30 am	Plenary Lecture 2 *Assoc. Prof. Dr. Elizabeth Davis* *Monash University, Australia* Title: Developing and Incorporating Learning Resources to Facilitate Active Learning in Pharmacology
9.30 am – 9.35 am	Break
9.35 am – 10.00 am	Symposium 1: Drug Metabolism Research Invited speaker: *Prof. Dr. Ong Chin Eng* *International Medical University* Title: Structure-Function Analysis of Cytochrome P450 Enzymes: Kinetic and Computational Modelling for Drug Clearance Prediction Symposium 2: Natural Products and Integrative Medicine Invited speaker: *Assoc. Prof. Dr. Wan Amir Nizam Wan Ahmad* *Universiti Sains Malaysia* Title: Flavonoids and Metainflammation in Diabetes
10.00 am – 10.15 am	Break

10.15 am – 11.15 am	Finalist 1: Oral presentations
	Finalist 2: Oral presentations
11.15 am – 11.30 am	Break
11.30 am – 12. 30 pm	Finalist 1: Shortlisted Poster presentations
	Finalist 2: Shortlisted Poster presentations
12.30 pm – 2.00 pm	Lunch Break
2.30 pm – 2.50 pm	Symposium 3: Cardiovascular Research
	Invited speaker: *Assoc. Prof. Dr. Satirah Zainalabidin Universiti Kebangsaan Malaysia*
	Title: The Action of SAC on Cardiac Remodelling in Myocardial Injury
	Symposium 4: Cancer Research
	Invited speaker: *Dr. Alan Yiu Wah Lee* *Monash University, Malaysia*
	Title: Exploration of the Tumor Suppressor Function of Semaphorin 5A in Brain Cancer Treatment
2.50 pm – 3.00 pm	Break
3.00 pm – 4.00 pm	Finalist 3: Oral presentations
	Finalist 4: Oral presentations
4.00 pm – 4.15 pm	Break
4.15 pm – 5.15 pm	Finalist 3: Shortlisted Poster presentations
	Finalist 4: Shortlisted Poster presentations

Day 3: 17th July 2021

9.00 am – 9.30 am	**Plenary Talk 3:** *Prof. Dr. Michael Fenech* *University of South Australia, Australia* **Title: Nutrigenomics from Laboratory to Clinical Practice**
9.30 am – 9.50 am	**Symposium 5: Neurological Diseases** **Invited speaker:** *Prof. Dr. Renu Agarwal* *International Medical University* **Title: Glaucoma and Neuroinflammation: Role of Magnesium-Based Compounds as Therapeutic Instruments** **Symposium 6: Metabolic Diseases** **Invited speaker:** *Assoc. Prof. Dr. Naguib Salleh University of Malaya* **Title: Ion channels in Endometrium: Their Roles in Uterine Fluid Regulation and Embryo Implantation**
9.50 am – 10:30 am	**Finalist 5: Oral presentations** **Finalist 6: Oral presentations**
10.30 am – 11.30 pm	**Break**
11.30 pm – 12.00 pm	**Awards Presentation** **Closing ceremony and remarks**

Personalized medicine: The link between people, animals & cells

Gordon H. Williams*

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The current models used to treat chronic medical conditions have at least four problems:

- The shift of burden from treatment of short-term diseases to chronic illnesses e.g. hypertension, diabetes, cancer.
- Current treatment model is failing: "Trial-and-error", time-consuming, exposure to unnecessary side effects, often clinically ineffective.
- Can lead to patient disengagement, non-adherence, and worse outcomes.
- Current practice based on population data and focused on treatment of symptoms/signs

Because of these shortcomings, there has been an emphasis on developing a personalized or precision medicine model where decisions are tailored to the individual patient. Two research approaches are being used to achieve this goal: Big Data and Person-Oriented. Big Data uses large patient populations (2-20 million) yielding massive clinical databases and large-scale genetic analyses of these individuals. It pools these data sets; applies mathematical approaches and generate insights that are not possible using standard analytics. Big Data's limitations are that it does not capture the impact of individual patient characteristics and environmental influences and clinical data may be unreliable. Working principles of a Person Oriented Medicine Approach are:

Chronic illnesses (e.g., hypertension, diabetes, anxiety, depression) are NOT diseases, but syndromes of a collection of individual diseases. The underlying mechanisms of these diseases can be determined by using a three-step individual assessment paradigm.

- Identify the specific mechanism of the individual disease using carefully created human cohorts, animal models and cells
- Identify the precise treatment/prevention for the disease
- Identify the specific person with the disease (genotype)

These approaches will be explored using hypertension as a model.

Keywords: Personalized Medicine, Big Data, Person-Oriented Medicine Approach, Hypertension

Things that bite and sting: The pharmacological characterization of animal venoms and toxins

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Venoms are a complex mixture of highly potent toxins that target key physiological processes. They play an important role in the capture and digestion of prey. Although humans are not perceived as 'prey' by venomous animals, we are often on the receiving end of life-threatening envenomings which are particularly prevalent in the South East Asian region. This is exacerbated by the fact that the Australasian and South East Asian regions are home to many of the world's most venomous terrestrial and marine animals. Although many monovalent and polyvalent antivenoms are available in the regions, many patients are treated with antivenoms that are not specific for the species responsible for the envenoming. Therefore, the clinical effectiveness of these antivenoms and the timing of administration to prevent/reverse symptoms is unclear. Our laboratory, in collaboration with researchers from other institutes, has undertaken an extensive examination of the venoms from many of these highly venomous creatures. This presentation will provide a brief overview of our work on whole venoms and isolated toxins, in particular, on the venoms of snakes and jellyfish. Our work has focused on the neurotoxic, cytotoxic and cardiovascular effects of these venoms, as well as the efficacy of commercially available antivenoms. We have utilized a number of in vivo and in vitro techniques including anaesthetized rats, isolated blood vessels, isolated skeletal muscle preparations and cell lines. Our research has provided important insights into the action of short-, long-chain postsynaptic and pre-synaptic neurotoxins, cytotoxins as well as key cardiovascular toxins affecting blood pressure. Our work has important implications for the successful management of envenoming.

Keywords: Antivenom, Snake venom, Jellyfish venom, Neurotoxin, Cytotoxin

Developing and incorporating learning resources to facilitate active learning in pharmacology

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In recent years, there has been an increasing expectation that University teaching moves away from the passive learning encouraged by the traditional didactic approach to content delivery, to incorporate more opportunities for active learning. With the emergency move to online teaching necessitated by the COVID-19 pandemic, the challenge has been to develop online learning resources that not only deliver required content, but that also facilitate active learning. At Monash University we have approached this in a number of ways. Content is delivered either asynchronously via "chunked" recordings or via interactive live lectures. Where content is delivered live, polling is used to engage students and frequent breaks are built into the session to allow time to check understanding and address areas of confusion. This content delivery is complimented by learning activities provided either as self-directed packages, or activits delivered synchronously with opportunities for peer-to-peer learning. These active learning resources have been developed using a variety of platforms including google forms, Moodle lessons and Lt (ADInstruments https://www.adinstruments.com/lt). Whichever platform is used, the aim is to use common design approaches that incorporate retrieval practice and checks of understanding. On completion, students are encouraged to reflect on their learning and to provide feedback on areas of confusion. This talk will provide examples of resources that have been developed for use in the teaching of pharmacology to medical students and science students.

Keywords: Active learning, Reflection, In-class polling, Content delivery, Teaching approaches

Nutrigenomics from laboratory to clinical practice

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Nutrigenomics is a modern field of nutritional science that is focussed on the impact of nutrients, specific foods and dietary patterns on gene expression, metabolism and maintenance of genome integrity. These effects are modulated by common and rare polymorphisms in genes that code for proteins involved in the uptake and transport of nutrients, and in the interaction of micronutrients with DNA, enzymes and structural proteins. It is evident from numerous intervention studies that metabolic response to a specific nutrient, food or dietary pattern varies substantially between individuals. There is, therefore, great interest in building the knowledge base to be able to predict precisely the nutrient and food combinations that an individual requires to "tune-up" metabolism to optimise cellular, organ, physical and mental function and to optimise regenerative capacity. In this presentation I shall (i) explain the use of human in vitro model systems to determine the optimal concentration of micronutrients for maintenance of genome integrity; (ii) discuss how human in vivo nutrition intervention studies can provide the data for predictive models that identify responders and non-responders based on their genome, metabolome, microbiome and other phenotypic characteristics; and (iii) describe current guidelines regarding the use of genetic data for personalised nutrition advice.

Keywords: Nutigenomics, Micronutrient, Metabolome, Personalised Nutrition Advice

Structure-function analysis of cytochrome P450 enzymes: Kinetic and computational modelling for drug clearance prediction

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Cytochromes P450 (CYPs) are a ubiquitous superfamily of enzymes responsible for the metabolism of a variety of compounds from vitamins to fatty acids to over 70% of commonly used drugs. The versatility of these enzymes in substrate catalysis has been explained in part by flexibility of the proteins and complexity of the binding mechanisms. Structure-function analysis of CYPs remains an area of intense research and numerous studies in this area have shed light on structural determinants of the substrate and inhibitor specificities and functional impact of genetic variants on drug metabolism and clearance. In this presentation, our recent works on structure-function analyses of CYP2D6, an important isoform involved in metabolism of antidepressants, neuroleptics, antiarrhythmics, beta-blockers, analgesics, and opiates will be presented. Common CYP2D6 alleles were characterized and analyzed using *in silico* modeling and *in vitro* enzyme kinetics. Site-directed mutagenesis was used to generate the allelic variants and enzyme kinetic studies were performed using high-performance liquid chromatography- or fluorescence-based assays using specific substrate and inhibitor probes. *In silico* modeling was employed using the published crystal structure of the human CYP2D6 as the template to create three-dimensional models of mutated CYP2D6 by homology modeling. Our studies indicate that mutations in some CYP2D6 variants tended to cause deleterious effect on catalysis, with reduced clearance for substrate probes. Inhibition studies with inhibitor probes however demonstrated non-uniformity in inhibitory patterns across different CYP2D6 variants, suggesting that inhibitor dependent intrinsic enzymatic differences exist among the investigated variants. Molecular docking indicated that some of the unique mutations in the variants, have negatively impacted activity by affecting ligand access and binding due to alteration of the substrate access channel and active site morphology. Considered together, these studies indicate that CYP2D6 variant selectivity for ligands was not solely governed by changes in the active site architecture induced by

the mutations, but that the intrinsic properties of the substrates and inhibitors also played vital role.

Keywords: Cytochromes P450, CYP2D6, In silico modeling, Enzyme kinetic studies

Flavonoids and metainflammation in diabetes

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Diabetes is responsible for 4% of all non-communicable disease deaths worldwide (WHO 2015). In Malaysia, one in every five adults has diabetes (DM), leading to an overall rise in prevalence from 13.4% in 2015 to 18.3% in 2019. (Institute for Public Health, 2020). Despite the high prevalence, diabetic patients' blood sugar control remains poor, raising questions about the effectiveness of available anti-diabetic medications. Obesity and hyperglycaemia are typical symptoms of type 2 diabetes (T2D). Obesity resulted in increased storage of lipids in tissues due to an abundance of free fatty acids (FFA). These factors can combine to cause significant changes in cell metabolism, including mitochondrial dysfunction, which will contribute to low-grade chronic inflammation (metainflammation). The latest therapeutic approaches to T2D have anti-inflammatory properties and their hypoglycaemic effects as the main modes of action. Anti-diabetic agents, including metformin, have inherent anti-inflammatory effects associated with their primary modes of action and are also associated with improving insulin resistance. However, prolonged therapies can lead to unwanted results, including lactic acidosis. Thus, merit to find alternative resources with minimal adverse effects but induces the effects alike metformin. Daily consumption of vegetables or plants has been linked to the prevention of diabetes mellitus. Furthermore, increasing the amount and variety of fibre-containing foods in one's diet will help to prevent many diseases of public health concern, such as obesity, cardiovascular disease, and diabetes. Locals in Malaysia have historically used the inflorescences of E. elatior to flavour food and for medicinal purposes. E.elatior flower is known to have a high content of flavonoids with inert anti-inflammatory and *in vitro* anti-diabetic properties. Our studies found that the crude aqueous extract of the flower reduced hyperglycaemia, body weight, and improved function and histopathological damage in the kidney of type 2 diabetic rat (T2DR), as well as having excellent *in vitro* anti-diabetic properties (Nor et al., 2019; Nor et al., 2020). The extract also has been shown to significantly reduced the

inflammatory marker, notably IL-6, in the kidney tissue of T2DR. Concurrently, the fibrotic markers (TGF-β and CTGF) also significantly reduced.

Keywords: Diabetes Mellitus, E. elatior flower, Metainflammation, Antidiabetic

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Nor NAM, Noordin L, Bakar NHA, Ahmad WANW. Evaluation of antidiabetic activities of *Etlingera elatior* flower aqueous extract *in vitro* and *in vivo*. J Appl Pharm Sci, 2020; 10(08):043-051. DOI: 10.7324/JAPS.2020.10805

The action of S-Allylcysteine (SAC) on cardiac remodelling in myocardial injury

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Myocardial infarction (MI) often triggers a series of compensatory processes driven by oxidative stress and inflammation known as cardiac remodelling. Cardiac remodelling is crucial for repair, replacement, and clearance of non-viable cardiomyocytes in infarcted areas. However, if unregulated, adverse cardiac remodelling may cause ventricular chamber dilatation and cardiac dysfunction that accelerates progression to chronic heart failure and sudden death in patients after MI. The events are driven by reactive oxygen species (ROS), renin-angiotensin system, inflammatory cells as well as various cell death pathways in the heart. Natural antioxidant supplement as an alternative in combatting free radical damage after an ischemic injury could be a promising strategy. Among all other emerging antioxidants, S-Allylcysteine (SAC); an aged-garlic compound has demonstrated cardioprotective effects. In fact, it has been reported that SAC possesses potent antioxidant, anti-inflammatory agent, as well as anti-fibrotic agent in various animal models. Interestingly, it has been proposed to confer cardioprotection also by stimulation of cystathionine-γ-lyase/hydrogen sulphide axis that ultimately increases antioxidant levels. With current ambiguous clinical strategy in re-establishing blood flow to the patients, thus this study is aimed to investigate the action of SAC on cardiac remodelling in MI rat model. In our lab, we investigated the impact of SAC therapy on adverse cardiac remodelling in a preclinical rat model in ex vivo and in vivo setting. For the ex-vivo experiment, an ischemia/reperfusion (I/R) model was used by using Langendorff setup. From the I/R model, our results found that reperfused hearts with SAC were shown to (1) prevent the aggravation of cardiac function after I/R induction, (2) dose-dependently upregulated glutathione reductase and glutathione level, and (3) reduce of LDH leakage and preserved mitochondrial permeability. To further confirm, the study was conducted in MI rat model induced by isoprenaline. Results found that SAC therapy to significantly (1) attenuate cardiac hypertrophy, fibrosis and oxidative, (2) prevented upregulation of angiotensin converting enzyme and angiotensin II type I receptor after MI. These findings altogether

suggested that SAC therapy reduced adverse cardiac remodelling after MI in rats. These findings highly suggest that SAC when sufficiently supplied to the heart would be able to prevent the deleterious complications after the ischemic insult. SAC therapy may be beneficial for management of adverse cardiac remodelling in patients after MI, thereby preventing heart failure and sudden mortality. However, a future study is warranted to further establish the effect of long-term intake of SAC and possible underlying mechanisms in preclinical animal models

Keywords: S-Allylcysteine, Cardiac remodelling, Antioxidant, Ischemia/reperfusion, Fibrosis, Oxidative stress

Exploration of the tumor suppressor function of Semaphorin 5A in brain cancer treatment

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Astrocytomas are the most common forms of brain tumor in human, among which glioblastoma mutliforme is highly malignant and exhibits high invasiveness and resistance to chemo- and radiotherapy, leading to high recurrence rate even after radical surgical resection of the tumor and a median survival of only 15 months after initial diagnosis. This calls for the development of novel effective treatment regimens, which apparently requires a more thorough understanding of the pathoetiology of glioblastomas at both cellular and molecular levels. Recently, accumulating evidence points to the emerging role of axon guidance molecules such as semaphorins, neuropilins and plexins in glioma progression. We have demonstrated the effects of semaphorin 5A (Sema5A) and its receptor plexin-B3 in inhibiting glioma cell migration, invasion and proliferation. Notably, analysis of clinical specimens revealed a marked decline in Sema5A protein level in high-grade human glioblastomas, suggesting a correlation between its loss of function and tumor progression. Restoration of Sema5A level by forced expression or exogenous supply of Sema5A protein successfully counteracts tumorigenicity of glioblastoma cells. These findings provide compelling evidence that Sema5A and plexin-B3 subserve anti-tumorigenic functions, which are compromised in glioblastomas due to a downregulation of Sema5A protein expression, hence contributing to high infiltration and malignancy. In this presentation, the mechanisms of tumor suppressor effect of Sema5A and the exploration of its therapeutic potential will be discussed.

Keywords: Astrocytomas, Semaphorin 5A, Receptor plexin-B3, Tumor suppresor

Glaucoma and neuroinflammation: Role of magnesium-based compounds as therapeutic instruments

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Ischemic retinal and optic nerve injury underlies several ocular conditions including glaucoma, the leading cause of irreversible blindness. Glaucoma is characterized by loss of retinal ganglion cells (RGCs). All current antiglaucoma medications primarily act by lowering elevated intraocular pressure (IOP), the major risk factor for glaucoma, and it is expected that RGC loss would be prevented secondary to IOP reduction. However, the disease progression often continues despite IOP lowering due to continued RGC loss. Glaucomatous RGC loss involves retinal ischemia that causes excessive glutamate accumulation and excitotoxicity. Excitotoxicity in turn causes oxidative and nitrosative stress and release of inflammatory cytokines due to intracellular Ca^{2+} overload in glial cells. Inflammatory cytokines promote pro-apoptotic signalling in RGCs via c-Jun and NFKB activation. Since magnesium is known to counteract ischemia, inflammation and oxidative stress, magnesium-based compounds could be potential therapeutic instruments for retinal disease involving similar pathophysiological processes. In our studies magnesium acetyltaurate (MgAT), a compound consisting of magnesium and taurine, was synthesized and its neuroprotective effects and mechanisms of action against endothelin-1 (ET1) induced retinal and optic nerve injury were investigated in *Sprague dawley* rats. MgAT was administered intravitreally as pre-, co- and post-treatment with ET1. Subsequently retinal expression of inflammatory markers, oxidative and nitrosative stress and RGC apoptosis were studied. Among 3 MgAT treatment groups, the MgAT pre-treatment was found to be most effective in preserving retinal and optic nerve morphology by restoring the expression of nitric oxide synthases and reducing nitrosative and oxidative stress. It was observed that MgAT pre-treatment prevents ET1 induced increase in retinal expression of interleukin (IL)-1β, IL-6, tumour necrosis factor (TNF)-α, c Jun, phospho c-Jun, NFKB and phospho NFKB. Furthermore, MgAT pre-treatment prolonged the RGC survival as observed

by retrograde labelling of RGCs using fluorogold as neuronal tracer as well as Brn3a immunostaining. We also subjected animals to visual function tests to determine the functional outcome of the neuroprotective effect of MgAT. Object recognition test using Morris water maze showed that MgAT pre-treatment abolishes the ET1 induced impairment of visual functions. In conclusion, magnesium-based compounds need further investigations due to their potential as therapeutic instrument against retinal and optic nerve diseases involving ischemia, inflammation and oxidative stress.

Keywords: Glaucoma, Neuroinflammation, Magnesium acetyltaurate, Oxidative Stress

Ion channels in endometrium: Their roles in uterine fluid regulation

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Embryo implantation is a complex process that requires a synchronization between embryo development into implantation-competent blastocyst and uterine development into receptive state. In humans, these events occur between days 19 to 22 of a 28 days menstrual cycle, under the influence of progesterone. Inadequate uterine receptivity and embryo development will result in implantation failure. During uterine receptivity period, signal exchange occurs between blastocyst and the receptive endometrium. At the same time, blastocyst is brought closer to the endometrium in order to initiate the embryo-endometrial contact. Animal studies have shown that this process involved changes in the electrostatic charge, however emerging evidence suggest that fluid loss from the uterine cavity can be the triggering factor. Fluid loss will result in embryo being sandwiched between the two opposing uterine walls, and hence, initiating the attachment phase of implantation. Uterine fluid loss involves multiple ion and water channels as well as membrane transporters that are exclusively expressed in the endometrium during the uterine receptivity period. Water escapes from the uterine lumen through the paracellular and transcellular routes which follows osmotic gradient created by NaCl movement. Studies in both humans and animals have shown that H_2O channel i.e., aquaporins (AQP), Na^+ channel i.e., epithelial sodium channel (ENaC) and Cl- channel i.e., Cystic Fibrosis transmembrane regulator (CFTR) are differentially expressed in the endometrium under different influence of sex-steroids i.e., estrogen and progesterone. Under progesterone influence, ENaC is up-regulated at the apical membrane of the endometrial epithelium, however, CFTR is down-regulated. Besides, AQP-2 which is expressed at the apical membrane such as AQP-2 is down-regulated, while AQP-5 and AQP-7 which are expressed at the basolateral membrane are up-regulated under progesterone influence. In the meantime, under progesterone influence, para-cellular fluid movement is prevented due to increase in tightness of the tight junction, with expression of tight junctional proteins such as claudin and occludin were also increased. Taken together, concerted actions of

progesterone favor the fluid to move out of the uterine lumen during the uterine receptivity period, thus ensuring adequate fluid loss that is required to initiate the first contact between blastocyst and the endometrium. Having perceived the important role of ion transport in achieving successful implantation partly contributed by fluid loss, studies have found that inhibiting the expression of these channels or transporters could interfere with normal uterine fluid movement, thus could result in failure of embryo implantation. In conclusions, precise regulation of fluid in the female reproductive tract is crucial for successful embryo implantation in which its dysregulation might results in infertility.

Keywords: Uterine fluid regulation, Sex-steroids, ENaC, CFTR, AQP

Anti-asthmatic effects of *Lignosus rhinocerotis* (Cooke) ryverdan extract: A potential alternative for allergic asthma management

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Asthma is a major public health issue that affects individuals of all ages, particularly children. The World Health Organization estimates that more than 235 million people are now suffering with asthma. Its prevalence is rising in many countries, including Malaysia. The disease is characterised by variable degrees of chronic inflammation, airway hyperresponsiveness and airway remodelling. Drug therapy, such as short acting β2-agonists, inhaled corticosteroids, and long acting β2-agonists, has become the most common treatment for asthma. These medications alleviate asthma episodes by relaxing the smooth muscle of the airways. However, asthma episodes and exacerbations can still occur since the treatment does not fix the underlying pathology, and long-term usage might result in adverse effects. These problems emphasise the necessity for an alternative asthma therapy. *Lignosus rhinocerotis* (Cooke) Ryvardan is a medicinal mushroom that has long been used by Malaysian indigenous people to treat asthma and other illnesses. Our research group investigated the therapeutic effects of *L. rhinocerotis* extract (LRE) on airway inflammation and remodelling in acute and chronic allergic asthma models. In this study, we demonstrated treatment with LRE significantly inhibited airway hyperresponsiveness (AHR) in house dust mite-induced mice. Histological findings revealed that LRE ameliorated ovalbumin (OVA)-induced histological changes by attenuating mucus hypersecretion and goblet cell hyperplasia in the lung tissues; as well as ameliorated airway remodelling by reducing smooth muscle thickness and the expression of TGF-β1 and Activin A positive cells in the lung tissues. LRE also significantly reduced the number of eosinophils and neutrophils in the BALF. Interestingly, a significant reduction of the FOXP3+ regulatory T lymphocytes was observed following OVA induction, but the cells were significantly elevated with LRE treatment. Subsequent analyses on gene expression revealed regulation of several allergic asthma

genes which were up-regulated following OVA induction but down-regulated following treatment with LRE. This study will give positive impacts to the society especially individuals suffering from allergic asthma. The use of LRE in addition to the existing asthma medications potentially a good strategy to maintain good symptom control and minimize the need for oral or inhaled corticosteroids. The reduce number of exacerbations will improve the quality of life by increasing productivity in the workplace, and school absenteeism in children. In conclusion, our findings suggest that LRE could be used as an alternative for the management of allergic asthma.

Keywords: Airway hyperresponsiveness, Allergy asthma, Inflammation, Lignosus rhinocerotis, Remodelling

Where pharmacology and venomics meet: Towards a comprehensive solution for snakebite envenomation—a priority neglected tropical disease

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Snakebite envenomation is a WHO-listed neglected tropical disease that kills more than 100,000 people yearly, while safe and effective antivenoms are lacking in many regions. Venomous snakes are highly diverse, and venom compositions can vary extensively between and within species, thus affecting the effectiveness of antivenom treatment. This study applied an integrated venomic strategy to unravel the diversity of snake venom compositions, followed by pharmacological and immunological methods to elucidate the ensuing functional consequences. Using the approach, more than fifty snake venoms from various species and localities in Asia have been investigated. In the series of cobra studies, the venoms of *Naja kaouthia* (Malaysia, Thailand, Vietnam), *Naja sumatrana* (Malaysia, Thailand, Indonesia), *Naja naja* (India, Pakistan, Sri Lanka), *Naja atra* (China, Taiwan), *Naja philippinensis* and *Naja samarensis* (The Philippines) were first analysed using C18 reverse-phase HPLC and nano-LC-tandem mass spectrometry, followed by data mining incorporating *de novo* venom-gland transcriptomics. The findings revealed significant phenotypic variations characterized by diverse key toxins, particularly the alpha-neurotoxins with variable sequences, antigenicity and expression levels. The alpha-neurotoxins were purified and shown to be highly lethal to mice (*i.v.* LD50 = 0.1–0.2 μg/g). The alpha-neurotoxins exhibited post-synaptic neuromuscular antagonistic activities in a chick biventer-cervicis nerve-muscle model, and a correlation between the toxin abundance and venom neurotoxicity was established. The long-chain alpha-neurotoxins (LNTX) constituted the main lethal components in *N. naja* (South Asia) and *N. kaouthia* (Thailand, Malaysia), whereas in the eastward dispersed species (*N. atra*, *N. philippinensis*, *N. samarensis*, *N. kaouthia* (Vietnam) and *N. sputatrix*), the short-chain alpha-neurotoxins (SNTX) were exclusively the predominant forms. Through antivenomics and toxin-specific neutralization study, SNTX

and LNTX were shown to be antigenically varied and differentially neutralized by antivenoms, revealing the limitation of efficacy in antivenoms used in the region. Accordingly, the neutralization potency of antivenom remains low against all cobras (*in vivo* potency <1 mg venom/ml antivenom), thus necessitating high doses in clinical treatment which will inevitably increase the risk of hypersensitivity reactions, treatment cost, and exhaustion of antivenom supplies. Further studies with venoms from kraits (*Bungarus*), king cobra (*Ophiophagus*), sea snakes (*Hydrophis*), sea kraits (*Laticauda*) and coral snakes (*Calliophis*) unveiled even wider inter-species and intra-species variations in the compositions, pharmacological activities and neutralization profiles of these neurotoxic venoms. Together, the determination of toxins unique to each species and its locale has broadened the project scope to develop snakebite diagnostics, and a prototypic antivenom through the use of a novel toxin immunogen mixture, appropriate adjuvant and improved immunization techniques in animals. It is envisaged that the promising outcome will pave the way for the development of a poly-specific, pan-regional antivenom with high efficacy, thereby contributing toward the WHO's vision to halve the global disease burden of snakebite by 2030.

Keywords: Antivenom, Neutralization, Proteomics, Transcriptomics, Venomics

Role of AMP-activated protein kinase in modulating perivascular adipose tissue function

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Perivascular adipose tissue (PVAT) is now recognized as an active endocrine and paracrine organ that modulates vascular function, with implications on the pathophysiology of cardiovascular diseases (CVD). In health, PVAT produces a wide range of adipokines with anti-contractile effect such as adiponectin. However, PVAT-derived adipokine profile is altered in obesity and CVD, leading to PVAT dysfunction. Alterations in AMP-activated protein kinase (AMPK) activity in the PVAT could be the underlying mechanism. This project aimed to determine the role of AMPK in modulating PVAT anti-contractile function. Experiments were conducted using wild type Sv129 (WT) and global AMPKα1 knockout (KO) mice. The anti-contractile effect of PVAT was studied using small wire myography in endothelium-denuded thoracic aorta rings either with or without PVAT. The relaxation responses of the aortic rings to a vasodilator, cromakalim, were subsequently assessed. Secretory function of the PVAT was tested using an immunoblotting array and ELISA. Relaxation responses to cromakalim in the WT mice were significantly enhanced in the presence of PVAT, an effect that was absent in vessels from KO mice. The KO mice PVAT secreted significantly less adiponectin. Addition of adiponectin augmented relaxation in both WT and KO mice aortic rings, while an adiponectin blocking peptide attenuated relaxation in WT but not KO mice aortic rings. Furthermore, high-fat diet-induced obesity reduced the anticontractile effect of PVAT, as well as reducing adiponectin secretion and AMPK activity. In conclusion, the study demonstrates that AMPKα1 has an important role in maintaining anti-contractile effect of PVAT, and this is likely to be mediated through adiponectin secretion. Obesity mimics many of the effects of AMPK knockout on PVAT function. Since AMPK is important for PVAT, targeting AMPK may have therapeutic potential in treating the deleterious effects of obesity on PVAT-derived adipokine profile and vascular function.

Keywords: Adiponectin, AMP-activated protein kinase, Obesity, Perivascular adipose tissue

OCA-01

Preliminary toxicity evaluation of novel quercetin 4´-cinnamate on HT29 human colon cancer cells

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In an effort to develop novel quercetin analogues with improved physicochemical as well as anticancer properties, quercetin 4´-cinnamate was generated in this study. It was chemically synthesized by attaching a cinnamic acid at the 4´-hydroxyl of quercetin. The cytotoxic and apoptotic effects of this novel compound on HT29 human colon cancer cells were evaluated by cell viability assay, fluorescence microscopy and flow cytometry; with concentration range of 12.5 to 200 μM and treatment duration of 24 to 72 h. Quercetin 4´-cinnamate showed significantly lower IC50 value (118.8 ± 22.4 μM) than quercetin (158.3 ± 4.8 μM) at 72 h. It induced apoptotic cell death. However, subsequent flow cytometry analysis showed that the abilities of quercetin and quercetin 4'-cinnamate to induce HT29 to enter either early or late apoptosis were not significantly different. Even though the lipophilicity and solubility of quercetin were previously shown to be improved by acylation with cinnamic acid, there was a delicate balance in which the permeability of the compound across the cell membrane was restricted by the bulkiness of the resulting acylated analogue. Due to such, even though quercetin 4´-cinnamate showed enhanced cytotoxicity against HT29, addition of an aromatic acid molecule to the quercetin core structure could cause the analogue to lose its ability to bind to the downstream modulators of apoptosis. Taken together, quercetin 4´-cinnamate synthesized in this study exhibited enhanced cytotoxicity against HT29 colon cancer cells, which warrants further investigation into the underlying non-apoptotic mechanisms and its therapeutic potential as a chemopreventive agent.

Keywords: Acylated quercetin analogue, Cinnamic acid, Cytotoxicity, Apoptosis, Lipophilicity, Solubility, Chemopreventive agent

OCA-03

Histopathological analysis of Pterostilbene as chemopreventive agent against lung squamous cell carcinoma in mouse model

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Lung cancer is one of the most common human cancers and lung squamous cell carcinoma (SCC) is the major type of lung cancer. Pterostilbene (PS) is a potential chemopreventive agent as it has been proven to exhibit anti-proliferative, anti-inflammatory, and antioxidant. Thus, this study was conducted to investigate the chemopreventive effect of PS against the N-*nitroso-tris-chloroethyl urea* (NTCU) induced lung SCC mouse model. A total of 24 female Balb/C mice at seven weeks of age were randomly categorized into four groups (n=6): that include two control groups: and vehicle control (VC) group and cancer group (NTCU); and two treatment PS groups: low dose of 10mg/kg PS + NTCU (PS10) and a high dose of 50 mg/kg PS + NTCU (PS50) groups. After 26 weeks of treatments, all mice were sacrificed, and the lungs were harvested for the tests. Histopathological observations of hematoxylin and eosin staining of the NTCU group showed the characteristics of SCC such as the formation of keratin pearls and increased nucleus/cytoplasm (N: C) ratio at the bronchial epithelium layer. The VC group still maintained the normal bronchial epithelium layer with a simple ciliated columnar similar to the PS 50 group. PS10 delayed the carcinogenesis of SCC at the pre-malignant stage with hyperplasia. Pterostilbene treatments significantly reduced the thickness of the bronchial epithelium layer and the expression of lung SCC marker of cytokeratin 5/6 compared to the NTCU ($p<0.05$). In conclusion, PS was able to prevent the development of lung SCC in mouse model.

Keywords: Pterostilbene, Carcinogenesis, Lung cancer, Squamous cell carcinoma, Cytokeratin 5/6

OCA-04

Effects of 1,4-BQ on DNA repair pathways and detoxification enzymes targeting hematopoietic stem/progenitor cells of different lineages

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Stem cells and hematopoietic progenitors (SSPHs) are major targets for benzene-induced hematotoxicity and leukemogensis. However, knowledge of the mechanism of benzene-induced toxicity targeting SSPH populations of different lineages is still limited. Thus, this study aimed to understand the effects of benzene exposure on HSPCs populations via lineage-directed strategies through toxicogenomic approaches. Mouse bone marrow (MBMCs) cells were exposed to benzene metabolite, namely 1,4-benzoinone (1,4-BQ) at concentrations of 0, 1.25,2.5,5,7 and 12 μM ex vivo for 24 h. Then genotoxicity profiles involving DNA repair pathways and detoxification enzymes were performed on different HSPCs consisting of myeloid, erythroid and lymphoid cells through colony-forming cell assay after 7 to 14 days of culturing. DNA repair pathways were assessed through analysis of DNA-PKcs and RAD51 proteins in which both are involved in non-homologous DNA repair and homologous DNA repair. The increase in DNA-PKcs in myeloid progenitors was observed to be significantly higher compared to other progenitors at all 1,4-BQ concentrations. Significant increases in RAD51 were observed only in myeloid (5 μM) and Pre-B lymphoid (7 μM) progenitors ($p > 0.05$). This is followed by assessment on the status of NQO1 detoxification enzyme and MPO metabolic enzyme. The results showed that myeloid progenitor cells were more sensitive to decrease in the detoxification mechanism of NQO1 and an increase in MPO by 1,4-BQ compared to other progenitor cells. In conclusion, 1,4-BQ toxicity is dependent on the type of progenitor cells which

is an important finding in understanding the mechanism of benzene-induced hematotoxicity and leukemogenesis.

Keywords: Benzene, 1,4-Benzoquinone, Hematopoietic Stem/Progenitor Cells, Lineages-specific, DNA-PKcs, RAD51, NQO1, MPO

OCA-05

miR-200c-3p promotes metastasis by binding to 3'-untranslated region of DLC1 in high grade serous ovarian carcinoma

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High-grade serous ovarian carcinoma (HGSC) is the most common ovarian cancer with highly metastatic properties. A small non-coding RNA, microRNA (miRNA) was discovered as a major regulator in many cancer metastases by regulating the expression of their targeted genes through their transcription binding motifs. Previously, we have proved that the aggressiveness of HGSC was due to over-expression of miR-200c-3p and down-regulation of its targeted gene, *Deleted in Liver Cancer 1* (*DLC1*). However, there was no data on the actual binding sites of miR-200c-3p to its targeted gene. The aim of the study is to provide functional evidence of miR-200c-3p and 3'UTR of *DLC1* interactions in a cell-based system. Luciferase reporter assay was performed in SKOV3 cell line co-transfected with vectors and miR-200c-3p mimic to confirm the binding action at the potential site as predicted by several databases. Based on *in silico* analysis, two putative binding sites were found within 3'UTR of *DLC1*. The luciferase reporter assay showed the conserved target binding motif at position 1367 to 1374 bp from the start of 3'UTR of *DLC1* transcript by significant reduction of luciferase activity compared to the control. However, no reduction of luciferase activity was observed in the assay using the mutated binding motif. These data proved that miR-200c-3p regulated *DLC1* expression post-transcriptionally by direct binding at 3'UTR and played a role in HGSC metastasis biology. Therefore, miR-200c-3p could be considered as a promising target for the therapeutic purpose.

Keywords: microRNA, miR-200c, Ovarian neoplasms, Target site, Luciferase assay, Metastasis, Epithelial-mesenchymal transition, 3'untranslated regions

OCA-06

The influence of breast cancer therapy on the expression of anti-neonatal Nav1.5 (nNav1.5) antibodies in the serum of breast cancer patients

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The role of voltage-gated sodium channels (VGSCs) in the progression of cancer is well established. Particularly, the neonatal isoform of Nav1.5 (nNav1.5) has been strongly associated with metastasis in breast cancer. In this study, we have aimed to understand the influence of breast cancer therapy on the expression of antibodies produced against nNav1.5. Around, 64 female breast cancer patients were recruited and grouped based on their treatment status: pre-treatment ($n=32$) and ongoing treatment ($n=32$) followed by the recruitment of 32 healthy female participants. Blood was withdrawn (consented) and the serum was separated. An in-house indirect ELISA assay was developed to detect the presence of anti-nNav1.5 antibodies in serum. Cytokine analysis was performed using magnetic Luminex assay. The expression of anti-nNav1.5 antibodies was highest in the serum of the pre-treatment group. The difference in the expression of anti-nNav1.5 antibodies in the serum samples of pre-treatment and ongoing-treatment group was significant ($P=0.0184$*). This implies that the expression of anti-nNav1.5 antibodies resonates with the metastatic condition displayed by pre-treatment group that did not receive any treatment. The improvement in the metastatic condition due to the influence of breast cancer therapy explains the downregulation of anti-nNav1.5

antibodies in the ongoing-treatment group. Cytokine analysis revealed a positive correlation (r=0.7260; *P*=0.0210*) between anti-nNav1.5 antibodies and Interleukin-6 (IL-6) in the pre-treatment group and a negative correlation (r=-0.8420; *P*-value=0.0040**) between anti-nNav1.5 antibodies and vascular endothelial growth factor (VEGF) in the ongoing-treatment group. In conclusion, the expression of anti-nNav1.5 antibodies, corresponding to the metastatic microenvironment, indicates the influence of breast cancer therapy on its expression level.

Keywords: nNav1.5, Breast cancer, Metastasis, Antibodies, Therapy, Cytokines

OCA-07

Potential use of a heat shock protein 90 inhibitor, geldanamycin, in combination therapy with cisplatin in oral squamous cell carcinoma

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Cisplatin is the chemotherapeutic agent of choice for oral squamous cell carcinoma (OSCC). Nevertheless, the occurrence of relapse in OSCC remains a major challenge due to the limited efficacy of chemotherapy in targeting a therapy-insensitive subpopulation in a heterogeneous tumour, known as cancer stem-like cells (CSCs). Therefore, the search for a better therapeutic strategy targeting both tumour bulks and CSCs is crucial for improving the treatment outcome in OSCC. In this work, we performed a high-throughput drug screening to rapidly identify potential drugs that can inhibit the viability of a CSCs model derived from OSCC SAS cell line. The CSCs model was derived via a sphere-forming assay, resulting in tumour spheres with stem cell-like characteristics. We treated the tumour spheres with a collection of compounds consisted of bioactive compounds and clinically approved drugs for 72 h. We further performed a second screening via multiple doses-response experiments to validate the identified candidate compounds. We also evaluated the effect of combination treatment of a promising validated compound with cisplatin on the tumour spheres. We found that 174 out of 1463 compounds significantly inhibited the cell viability of the tumour spheres. The validation screening showed that geldanamycin, an inhibitor of heat shock protein 90, exerted a highly inhibitory effect on the viability of the tumour spheres. The compound also synergized the cell viability inhibition

effect of cisplatin against the tumour spheres. Herein, we highlighted the potential use of geldanamycin in combination therapy with cisplatin in OSCC for eradicating both cisplatin-sensitive and -insensitive cancer cells.

Keywords: Oral squamous cell carcinoma, Cancer stem-like cells, Cisplatin resistance, High-throughput drug screening, Drug combination therapy

OCA-08

Evaluating experiences of cancer patients: A hospital based qualitative study from Mauritius

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Various cancer care studies have indicated that during cancer diagnosis, patients and their families encounter several hardships such as economic crisis, instability in relationships, increased level of mental agony, changes in quality and way of life. Patients have expressed intense grieve and skepticism on their initial diagnosis. Therefore, it is crucial to understand the paradigm of cancer care in the treatment and its implementation, thus augmenting the treating oncologist about the patient's mental disposition. This study examines patient's experiences upon their visit to the cancer clinic and psychological hassle after diagnosis and through the course of treatment. A phenomenological qualitative study was conducted at the Oncology Department of Candos Hospital, Mauritius, from August to September 2019. NVivo 12 Plus software was used for thematic analysis. Study participation was elective, and written consent was taken from all participants. Data was collected via an extensive one on one interview basis and was recorded, and an authoritative sampling technique was used. On the whole, seven females and five males participated. Seven main themes such as motivational influences, cognitive factors, community, message for others, disease awareness, economic factors and perceptivity towards the healthcare systems were derived from 25 codes. The main inference from this study was the lateral thinking skills of informal caregivers and healthcare professionals towards the patient's sentiments and psychological reactions regarding their cancer experience. Caregivers' positivity was directly correlated with patients' treatment compliance, resulting in positive outcomes and decreasing the psychological consequences.

Keywords: Cancer Care Facilities, Emotional Intelligence, Empirical Research, Health Status, Professional-Patient Relations, Psychiatry and Psychology Category

PCA-01

Rho-associated kinase (ROCK) signaling pathway activated in response to increased tissue rigidity in lung squamous cell carcinoma (SCC) *in vivo*

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Increased tissue rigidity is an emerging hallmark of cancer as it can promote cancer growth. Increased tissue rigidity was found to promote cancer growth by activating Rho-associated kinase (ROCK) signalling pathway in several cancers. However, the characterization of their relationship in lung squamous cell carcinoma (SCC) remains elusive. This study aimed to evaluate the relationship between tissue rigidity and ROCK signalling pathway in lung SCC using mouse model. BALB/c mice were allotted into two groups (n=8); Vehicle (receiving 70% acetone) and cancer group (receiving 0.04M N-nitroso-tris-chloroethylurea). The treatment was given at the dorsal area of mouse's shaved skin, twice a week for 30 weeks. After termination of mice, Hematoxylin & Eosin staining was performed to confirm the formation of lung SCC. Immunohistochemistry staining for ki67 protein and Sirius red staining were also performed to determine the proliferation status and collagen content respectively. After that, western blot was performed on lung tissues to evaluate ROCK signaling pathway expression. P-value of ≤ 0.05 was assigned as statistical significance. We found a significantly higher ($p<0.05$) epithelium thickness, proliferative activity, and collagen content in cancer group as compared to vehicle group. Meanwhile, RhoABC, ROCK1, and ROCK2 protein expression were found to be significantly higher ($p<0.05$) in cancer group as compared to vehicle group, which may indicate a relationship between increased tissue rigidity and ROCK signaling pathway activation in lung SCC.

Increased tissue rigidity may be responsible for promoting cancer growth by activating ROCK signaling pathway in lung SCC.

Keywords: Lung squamous cell carcinoma (SCC), Rho-associated kinase (ROCK), Tissue rigidity, Epithelium thickness, Cell proliferation, Collagen

PCA-02

Antioxidant activity of pterostilbene in lung squamous cell carcinoma *in vivo*

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Pterostilbene has shown various pharmacological roles including anticancer, anti-inflammatory and antioxidant. Non-small cell lung cancer (NSCLC) consists of three main subtypes which are lung adenocarcinoma, lung squamous cell carcinoma (SCC) and large cell carcinoma (LCC). Although there have been several studies being done using pterostilbene in NSCLC, data on the antioxidant activity of pterostilbene in lung SCC via in vivo model remained limited. Hence, this study aimed to determine the antioxidant activity of pterostilbene in lung SCC In Vivo. Initially, Balb/C mice were divided into 4 groups consist of 2 control groups (vehicle control, VC and cancer control, LC) and 2 pterostilbene treatment groups (10 mg/kg, PS10 and 50 mg/kg, PS50). The lung SCC In Vivo model was developed by topically application of 0.04M N-nitroso-tris-chloroethylurea (NTCU) on the upper dorsal of the mice. The antioxidant parameters including glutathione (GSH) and superoxide dismutase (SOD), with oxidant markers such as malondialdehyde (MDA) and protein carbonyl (PC) were measured in this study. The SOD and GSH levels in PS50 were significantly higher ($p<0.05$) than in the LC group. Moreover, both PS10 and PS50 showed a significant reduction ($p<0.05$) of MDA and PC levels as compared to LC group. In conclusion, pterostilbene has shown to play a central role as antioxidant by reducing the oxidative stress level in lung SCC In Vivo, making it as a potential chemopreventive agent for lung SCC.

Keywords: Pterostilbene, Lung cancer, Lung squamous cell carcinoma, Antioxidant

PCA-03

The novel molecular imaging markers of 18F-Fluorocholine PET/CT with expression of CD47, miRNA-21 and miRNA-155 in underpinning breast cancer

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18F-Fluorocholine uptake increases during malignant transformation and potentially identify the aggressiveness of cancer cells. However, the novelty of the 18F-FCH with expression of miRNA and CD47 were sought as there were exceedingly scare report on their role in underpinning aggressive breast cancers. We examined the ability of 18F-FCH uptake with expression of CD47 and miRNA in detecting aggressiveness of breast cancers. Twenty-one breast cancer patients with BIRADS 4 or 5 on mammogram criteria were recruited and underwent 18F-FCH PET/CT. Histological results were used as gold standard. The standardized uptake value (SUV max) was analysed to determine the degree of altered choline metabolism on Positron Emission Tomography. The expression of miRNA was measured using quantitative real-time polymerase chain reaction. After the PCR cycles, melting curve analyses were performed to validate the specific generation of the expected PCR product by looking at the upregulated (miRNA expression) or downregulated (low miRNA expression). While CD47 expression were analyzed by using ELISA and the standard curve were construct using regression analysis. This study showed that high SUV max of 18F-FCH is associated with expression of mirna-21 in lymph node with means of 1.81 ± 2.21g/dl, $p=0.05$ and metastasis with means of 3.33 ± 3.61g/dl, $p=0.02$, while mirna-155 in lymph node with

means of 1.47±1.99g/dl, p=0.01. Furthermore, there is correlation between high SUV max with means of 1.28±1.90g/dl and expression of CD47 with means of 0.85±0.23g/dl in lymph node, p=0.008. 18F-FCH with expression of miRNA and CD47 are novel predicting markers in underpinning aggressive breast cancers.

Keywords: [18f]-fluorocholine, Computed tomography, Positron emission tomography, [18f]-mirna, CD47

PCA-04

The effects of different coating substrates on human primary lung cancer cells growth

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Primary lung cancer cells are generally anchorage-dependent and attach to the extracellular matrix in order to grow and proliferate. However, the cells' characteristically weak adherence to the tissue culture surface has impeded their cell survival rates and presents technical limitations to the design of experiments. Hence, the use of suitable coating substrate needs to be identified to improve the growth and attachment ability of these cells. Following biopsy, the isolated cells were incubated with Airway Epithelial Medium supplemented with 10% fetal bovine serum and 1% penicillin-streptomycin solution in T-25 flask. The samples were incubated in 3 different coated substrates (collagen, gelatin and poly-L-lysine) with non-coated flask as control. Cells were added after the coating procedures were done per recommendation by Sigma (USA). Briefly, 2.5mL of collagen type 1 and gelatin solution was left for 30 and 120 minutes in the flask respectively while 1mL of poly-L-lysine added to the flask for 5 minutes before rinsed with sterile water and allowed to dry for 2 hours. Then, growth and morphology of the cells were observed under inverted microscope and maintained for 14 days. Monolayer attachment and epithelial-like morphology were only observed in flasks coated with collagen type 1 solution (n=6) starting day 14. The others showed no growth after 14 days of incubation. Primary lung cancer cells have grown well in AEM with collagen type 1 as a coating substrate. Collagen serves as an anchor and substrate for the cells to grow, proliferate and survive.

Keywords: Coating substrate, Primary lung cancer, Collagen type 1, Cell culture, Lung cancer

PCA-07

Exploring the cytotoxic mechanisms of pediocin PA-1 towards HeLa and HT29 cells by comparison to known bacteriocins

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The purpose of this study was to explore potential mechanisms of cytotoxicity towards HeLa and HT29 cells displayed by Pediocin PA-1. We did this by carrying out sequence alignments and 3D modelling of related bacteriocins which have been studied in greater detail: Microcin E492, Enterocin AB heterodimer and Divercin V41. Microcin E492 interacts with Toll-Like Receptor 4 in order to activate an apoptosis reaction, sequence alignment showed a high homology between Pediocin PA-1 and Microcin E492 and 3D modelling showed Pediocin PA-1 interacting with TLR-4 in a way reminiscent of Microcin E492. Microcin E492 has several different mechanisms of cytotoxic effects and based on the high homology between Pediocin PA-1 and Microcin E492, we suggest, based on additional studies of Pediocin PA-1, that it does indeed have at-least a dual-mechanism of action. Furthermore, Pediocin PA-1 had the highest homology with the Enterocin heterodimer, an apoptosis inducing molecule, particularly chain A. Both Pediocin and Enteorcin A contain cysteine residues which form disoluphide bonds in order to stabilise structure. Based on this we are led to strongly believe Pediocin PA-1 interacts with TLRs in order to cause cell death. If this is the case it would explain the difference in cytotoxicity towards HeLa over HT29 cells, due to relative over- and under-expression of particular TLRs in both HeLa and HT29 cells. Overall, we believe Pediocin PA-1 exhibits a dual effect acitvating not only TLRs, but also targeting of lipid vesicles, which is dose dependant, like that of Microcin E492.

Keywords: Cancer, Cervical, Colon, Bacteriocin, Therapeutics, Novel, Apoptosis, Bionformatics

OCVS-01

Transcutaneous vagus nerve stimulation: Investigation on cholinergic anti-inflammatory pathway in rats with isoprenaline induced myocardial infarction

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Myocardial infarction (MI) is characterized by sudden ischemic death of cardiomyocyte due to occlusion of coronary vessels. Upon the onset of MI, inflammation takes place to remove necrotized cardiomyocytes, however this process is slow and results in prolonged inflammation which can depresses cardiac function. Increasing evidence have suggested that the modulation of vagus nerve (VN) can attenuate the inflammation associated with MI, nevertheless the underlying cardioprotective mechanism remains to be elucidated. This study aims to examine the cardioprotective mechanism of transcutaneous vagus nerve stimulation (tVNS) by looking into cholinergic anti-inflammatory pathway (CAP) and the macrophages polarization. MI was induced with subcutaneous injection of isoprenaline hydrochloride (85mg/kg) for two consecutive days. VN was stimulated by applying electrical stimulation at tragus with stimulation intensity of 20Hz, 0.2ms, 2mA, one hour daily for two weeks. Left ventricular contractility was then assessed through Langendorff experiment by analyzing parameters such as left ventricular developed pressure (LVDP), maximum dp/dt and minimum dp/dt. Improvements of LV contractility were observed based on increased value of LVDP, maximum dp/dt and minimum dp/dt of MI+tVNS compared to negative control. Nonetheless, this improvement was abolished by the administration of atropine as LVDP, maximum dp/dt and minimum dp/dt of MI+tVNS+Atropine were lower compared to MI+tVNS. Conversely, MI+Sham Stimulation did not show any improvements of LV contractility. We postulated that the cardioprotective mechanism was attributed to the activation of CAP

via VN stimulation. In the future, we will examine the effects of tVNS on cardiac inflammation, adverse cardiac remodeling and macrophage phenotype.

Keywords: Myocardial Infarction, Transcutaneous Vagus Nerve Stimulation, Left Ventricular Contractility, Cholinergic Anti-inflammatory Pathway, Macrophage Polarization

OCVS-02

The effect of 17βH-neriifolin on the cardiac structure and function in cardiac hypertrophy rat model

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Cardiovascular disease is the leading cause of death in Malaysia. Cardiac glycosides such as digoxin has been commonly used for heart failure patients, however, its toxicity remains as a main concern due to its side effects. Recently, a cardiac glycoside compound which inhibits Na^+-K^+-ATPase in vitro identified as 17βH-neriifolin (SNA 209) has been isolated by FRIM. Thus, this study was aimed to investigate the potential use of SNA 209 as a treatment for isoprenaline (ISO)-induced cardiac hypertrophy rat model. Male Wistar rats (200-250g, n=56) were randomly divided into seven groups. Cardiac hypertrophy was induced by ISO (10 mg/kg/s.c) for 14 days followed by SNA 209 treatment (2.5mg/kg or 5 mg/kg; orally) for 14 days. Control rats were given saline as vehicle for ISO, and DMSO as vehicle SNA 209. Statistical analysis was performed by using one-way ANOVA and $p<0.05$ was considered as significant. Systolic blood pressure (SBP) via tail-cuff method in ISO groups were all significantly increased compared to control group ($p<0.05$), and SNA 209 treatment managed to reduce the SBP. Besides that, SNA 209 treatment also reversed the decrease in rat's heart rate (HR) significantly in ISO rats. The cardiac injury marker (pro-BNP) level was remarkably reduced by SNA 209 in ISO group. Cardiac hypertrophy was evident by the increased left ventricle size and cardiomyocytes size. The left ventricle developed pressure (LVDP) in ISO treated with SNA was raised significantly vs ISO group. In conclusion,

SNA treatment was able to improve the cardiac function and structure; hence, the potential use of SNA 209 as treatment for hypertrophy which is one of the features of heart failure condition.

Keywords: β adrenoceptor, Isoprenaline, Cardiac hypertrophy, Fibrosis, Heart failure

OCVS-03

Haptoglobin as a potential biomarker to predict coronary artery disease in young adults with hypertension and prehypertension

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Coronary artery disease (CAD) risk among young adults with hypertension and prehypertension tend to be underestimated as the young age is considered as a protective factor. Hence apart from conventional risk factors, novel biomarkers discovery is essential to improve the accuracy of CAD risk stratifications in hypertensive and prehypertensive young adults. In this study, we investigated the association between acute myocardial infarction (AMI) and haptoglobin in hypertensive and prehypertensive young adults to determine the potential role of haptoglobin in predicting CAD in these cohorts. This was a cross-sectional study involving 160 male aged $\leq$ 45 years old, consisting of 40 subjects in each control, prehypertensive, hypertensive and AMI group. Blood samples were collected from all subjects. Plasma concentrations of haptoglobin were measured using enzyme-linked immunosorbent assay (ELISA). The mean age for control, prehypertensive, hypertensive and AMI group were 37 $\pm$ 5, 35 $\pm$ 7, 33 $\pm$ 7 and 33 $\pm$ 5 years respectively. Mean plasma concentration of haptoglobin in the AMI group was significantly increased as compared to the hypertensive, prehypertensive and control groups (290.63 $\pm$ 99.90 vs. 208.47 $\pm$ 112.93 vs. 175.05 $\pm$ 110.17 vs. 170.02 $\pm$ 108.11 ng/ml, $p<0.006$) respectively. Multinomial logistic regression showed that haptoglobin in prehypertensive and hypertensive young adults was significantly

associated with AMI (OR: 0.981, 95% CI: 0.969-0.993, p=0.002, and OR: 0.985, 95% CI: 0.985-0.973, p=0.017), independent of other conventional risk factors. High plasma concentration of haptoglobin is a potential biomarker to recognize hypertensive and prehypertensive young adults with high risk of developing CAD.

Keywords: Coronary artery disease, Hypertension, Prehypertension, Young adults, Biomarker

OCVS-04

Modulation of endothelial nitric oxide synthase (eNOS) by epigallocatechin gallate (EGCG) for the treatment of vascular dysfunction in angiotensin II-infused hypertensive mice

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Studies in recent years have shown that ingestion of epigallocatechin gallate (EGCG), provides beneficial effects in hypertensive patient. However, the effect of EGCG in improving vascular relaxation in hypertensive subjects with compromised renin angiotensin-aldosterone system (RAAS) has not been elucidated. The present study aims to investigate if EGCG improves vasorelaxation via attenuation of eNOS uncoupling in angiotensin II-infused hypertensive mice. C57BL/6J mice (8-10 weeks old) were randomly divided into four groups namely control, control treated with EGCG (50mg/kg/day, oral gavage), angiotensin II (1.2mg/kg/day) and angiotensin II treated with EGCG. The average systolic blood pressure (SBP) of the mice was measured every three days. After the treatment period, vascular function was investigated by assessing the relaxation of the aortic rings of the animals to acetylcholine (3 nM–10 μM). The level of nitric oxide (NO), cyclic guanosine monophosphate (cGMP), tetrahydrobiopterine (BH4), reactive oxygen species (ROS) and NADPH oxidase-2 (Nox-2) in vascular tissues were also determined. *In vivo* treatment with EGCG for 14 days attenuated the increase in SBP, improved the impaired vascular relaxation, decreased NO level, increased the vascular, cGMP and BH4 level significantly in angiotensin II- infused hypertensive mice. Treatment with EGCG also significantly decreased the elevated level of ROS

and Nox-2 protein in angiotensin II-infused hypertensive mice. Treatment with EGCG improves vasorelaxation in angiotensin II- infused hypertensive mice may be attributed partly to its effect in attenuating eNOS uncoupling via modulation of oxidative stress.

Keywords: Renin angiotensin-aldosterone system, Endothelial dysfunction, Reactive Oxygen Species, Hypertension, Epigallocatechin gallate

OCVS-05

The potency of navitoclax in mediating the viability of human umbilical vein endothelial cells

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Pathological angiogenesis involved endothelial cells proliferation and migration which can deteriorate cancer and atherosclerosis. Navitoclax is proposed as an effective pro-apoptotic agent against cancer cells as it could stop cancer metastasis. It acts on Bcl-2 family proteins which able to regulate cell survival. Cell survival signal activation contributes to atherosclerosis progression that can be a novel therapeutic target for atherosclerosis treatment. However, research of navitoclax on endothelial cells is still scarce due to a limited cytotoxicity report. This study demonstrates the navitoclax efficacy in modulating human umbilical vein endothelial cells (HUVECs) viability at different concentrations and treatment times. The navitoclax concentrations starting from 0.2 to 3.0μM at four-time points; 18-, 24-, 48- and 72-hours were used. The cell viability percentage after the treatment was calculated and the drug dose reduces 50% of cell viability (IC50) was determined. The IC50 value for 18-hours post-treatment was undefined due to low efficacy at a limited treatment time. While for 24-, 48- and 72-hours, the IC50 values were 0.91μM, 0.72μM, and 0.12μM respectively. Shrinkage cells were observed after 24-, 48- and 72-hours treatment of 3.0μM navitoclax indicates cell viability reduction induced by navitoclax. The navitoclax anti-survival effect was augmented at the highest concentration with a longer treatment time, hence, suggests its potency against HUVECs to be time- and

concentration-dependent. These results indicate navitoclax is safely utilized against HUVECs for *in-vitro* angiogenesis model which represents advanced atherosclerosis condition. Lastly, 0.9μM navitoclax at 24-hours treatment time is relevant to exhibit an optimum efficacy against HUVECs.

Keywords: Cell viability, HUVEC, IC50, Navitoclax, Pro-apoptosis, Efficacy

OCVS-06

S-Allylcysteine limits cardiovascular injury induced by isoprenaline in ovariectomized rats

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Post-menopausal women are more susceptible towards cardiovascular disease; however, current therapy has its drawbacks. Sources with high anti-oxidant properties are sought as possible new drug discovery. This study was aimed to study the effects of S-Allylcysteine (SAC) on the isoprenaline-induced myocardial injury (MI) in ovariectomized (OVX) rats. Forty female Wistar Rats were acclimatized before subjected to bilateral ovariectomy (n=32) and Sham procedure (n=8). After three-week recovery, the rats were injected subcutaneously with isoprenaline (85 mg/kg) or normal saline, twice daily within 24 hours interval. The rats then received either S-Allylcysteine (100 mg/kg, p.o.) or distilled water for one week. Electrocardiogram and blood pressure were monitored. During sacrifice, the hearts were cannulated on Langendorff apparatus for cardiac function. The serum and body organs were stored for further analysis. The uterine weight was reduced significantly in OVX rats, although their serum estradiol level was unaltered. Serum troponin-T and ECG tracing showed a marked cardiac injury in MI group when compared to non-MI group. Meanwhile, systolic BP in OVX rats reduced significantly after receiving SAC. OVX+MI rats given with SAC showed a significant difference compared to other groups in antioxidant glutathione level. Picrosirius red staining was observed in MI-induced rats' hearts, indicating marked fibrosis and it was reduced in the rats that received S-Allylcysteine. The results were analyzed using ANOVA and $p<0.05$ was considered as significant. S-Allylcysteine could limit MI in estrogen-deficient rat model. Further studies are warranted to investigate the underlying mechanism as a possible clinical treatment.

Keywords: Cardiovascular, S-Allylcysteine, Ovariectomy, Cardiac Function, Antioxidant

OCVS-07

Cardioprotective role of (-)-hydroxycitric acid by attenuating the TLR4/NF-kβ/NLRP3 pathway in high fat diet/low dose of streptozotocin-induced diabetic cardiomyopathy in rats

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Obesity is closely related to the development of cardiovascular risk factors including dyslipidemia and type 2 diabetes. Hydroxycitric acid (HCA), a major active compound in *Garcinia cambogia* extract. In animal and human research, HCA has been proven to inhibit body weight gain and fat accumulation. We hypothesized that HCA may aid in the prevent the body weight gain and cardiovascular risk factors. To elucidate the mechanism of action of HCA, rats fed with high fat diet and low dose of streptozotocin (STZ) to develop type 2 diabetic conditions. Four groups were used in the experimental research. Group I consisted of normal control animals. Group II rats fed with high fat diet and injected with low dose of STZ (35 mg/kg) (diabetic control). Group III, diabetic rats were given 50 mg/kg body weight of HCA, whereas group IV diabetic rats were given 100 mg/kg body weight of HCA, orally 28 days. Blood glucose, insulin, HbA1C, lipid profile, and oxidative stress markers were measured biochemically. In addition, we estimated mRNA expression, immunohistochemistry, and immunofluorescence to look at a variety of inflammatory markers. Diabetes rats treated with HCA demonstrated significant reduction in body weight, hyperglycemia, and HbA1C levels, as well as elevated insulin levels, changes in lipid profile and antioxidant status. Following HCA treatment, diabetic rats exhibited reduced inflammatory markers (TLR4, MYD88, NF-kβ, IKKβ, and NLRP3), as determined by mRNA expression, immunohistochemistry, and immunofluorescence. Thus, based on the findings, HCA may be considered a preventive antidiabetic medication in the prevention of diabetic cardiomyopathy in rats.

Keywords: (-)-Hydroxycitric acid, Cardioprotection, Diabetes mellitus, TLR4/NF-kB/NLRP3

OCVS-08

Novel insight into the role of oxidant activation of Protein Kinase G in resistance artery vasodilation

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A healthy endothelium is vital for cardiovascular health. Within the endothelium of resistance arteries, vasodilatory pathways are predominantly dependent on localised calcium (Ca^{2+}) signalling. These endothelial cells (ECs) Ca2+ signals control potassium (K^{+}) channel activity that regulates arterial membrane potential. A prominent dilatory protein, Protein Kinase G (PKG) can be activated by oxidant and the downstream dilatory mechanisms is different to its classical activation by cGMP. This research delineates the role of oxidant activation of PKG and Ca^{2+} pathways in the endothelium. Effects of oxidant-activation of PKG on Ca^{2+} signalling pathways were assessed via the use of a genetically modified mouse model whereby an amino acid switch (Cysteine to Serine) renders Protein Kinase G insensitive to oxidant activation (PKG[C42S]KI). Mice were euthanised by cervical dislocation, in accordance with the UK Home Office Guidance on the Operation of the Animals (Scientific Procedures) Act 1986. EC Ca^{2+} signals were visualised using high-speed (50Hz) spinning disc confocal microscopy of third-order mesenteric arteries which were slit open and imaged in an en-face configuration and pressure myography/ Overall findings shows an impaired vasodilation to acetylcholine, TRPV4 activator, GSK101 yet a normal function of intermediate and small KCa^{2+} channels. The findings are in line with the endothelial imaging whereby increased IP3-pulsar frequency and TRPV4 Sparklets activity was higher in normal arteries compared to arteries that are insentitive to oxidant activation of PKG. From our data, it is suggested that oxidant-activation of

PKG plays a role in the upstream pathway of M3 muscarinic induced dilation within the endothelium. The principal vasodilatory pathways of the small artery endothelium are critically dependent on oxidant generation which activate PKG.

Keywords: Small resistance artery, Blood pressure regulation, Oxidant, Protein kinase G(PKG), Pressure myography, *En face* calcium imaging

OCVS-09

Malaysian octogenarians with acute coronary syndrome: Ten-year change in management and outcome

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Octogenarians are known to have a higher risk of mortality due to acute coronary syndrome (ACS) but are often less aggressively managed than younger patients. This study aimed to investigate the 10-year change in ACS management and outcome for octogenarian patients in Malaysia. The Malaysian National Cardiovascular Database-ACS (NCVD-ACS) registry was used to identify patients aged 80-years-old and above admitted with ACS in the year 2008 (n=117) and 2017 (n=543). Changes in coronary intervention, pharmacotherapies and 1-year all-cause mortality were examined. Survival analysis was performed using Cox proportional hazard regression. The admission for ACS in octogenarians increased more than 4-folds between 2008 and 2017 (p<0.05). The rates of percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) were 6.9% and 0.2%, respectively, in 2017, with no significant change compared to 2008 (PCI= 5.1%; CABG= 0%). The rates for in-hospital prescription of cardiovascular pharmacotherapies in 2017 were as follows: aspirin (96.7%), DAPT (88.9%) and anticoagulants (88.2%) with significant increases observed compared to 2008 (p<0.001). The outcome of 1-year-mortality improved by 7.4% in 2017 compared to 2008 but not significantly (47.0% 2008; 39.6% 2017, p=0.139). Higher risk of 1-year-mortality for octogenarians was found if they were prescribed with ACEi/ARB and beta blocker (HR> 1; P<0.05). In conclusion, significant improvement

in pharmacotherapies and mortality outcomes were observed in Malaysian octogenarians with ACS when comparing two time points in the ten years. There is little change in coronary intervention, reflecting clinical preference in these vulnerable population.

Keywords: Cardiovascular Disease, Mortality, Intervention, Pharmacotherapies, Pharmacoepidemiology

OCVS-10

The interaction between sympathetic nerves and perivascular adipose tissue-derived mediators under standard and low oxygen levels

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It is well accepted that perivascular adipose tissue (PVAT) is a source of numerous important vasoactive compounds. Despite this, information on the link between PVAT-derived mediators and the neurovascular system is still sparse. The present study investigated the effect of adrenergic activation on the release of PVAT-derived mediators, under standard experimental oxygen and low oxygen conditions. Rat mesenteric arterial beds (either with or without PVAT) were perfused under standard (95 % O_2 and 5 % CO_2) and low/hypoxic (95 % nitrogen (N_2) and 5 % CO_2) oxygen conditions. Perfusate was collected at basal tone conditions (control) and during the electrical field stimulation (EFS) evoked vasocontractile responses. Multiplex assay was carried out for measuring adipokines (adiponectin, leptin, interleukin-6, monocyte chemoattractant protein-1, tumour necrosis factor-alpha, interleukin beta and total plasminogen activator inhibitor-1) release. In the presence of PVAT, the level of interleukin-6 release increased under low oxygen conditions but absent under standard oxygenation. Under low oxygenation, the activation of sympathetic nerves modulated the release of PVAT-derived leptin. The present study provides evidence that the activation of sympathetic nerves in PVAT can modify PVAT-derived mediator(s) release, hence contributes to the regulation of vascular tone.

Keywords: Perivascular adipose tissue, Sympathetic, Mediators, Oxygen, Leptin

PCVS-01

Investigation of the vasoprotective mechanism of epigallocatechin-3- gallate (EGCG) in Spontaneously Hypertensive Rats

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Epigallocatechin-3-gallate (EGCG), the major catechin found in green tea has been demonstrated to potentially reduce the risk factors for cardiovascular disease. EGCG has been shown to lower the blood pressure of hypertensive animals but whether the decrease is contributed by its vascular protective mechanism is yet to be elucidated. Therefore, the current study investigated the vasoprotective action of EGCG in hypertensive animals. Wistar-Kyoto (WKY) rats and Spontaneously hypertensive rats (SHR) were divided into four groups namely WKY Control, SHR Control, SHR treated with EGCG (50mg/kg/day) and SHR treated with Losartan (10mg/kg/day) and treatment was given for 4 weeks by daily oral gavage and the blood pressure was monitored by tail-cuff method every 3 days. Acetylcholine-induced endothelium-dependent and sodium nitroprusside-induced endothelium-independent relaxations were assessed in isolated aortic rings at the end of treatment following phenylephrine contraction. After 4 weeks of treatment, systolic blood pressure significantly decreased in SHR treated with EGCG and Losartan group compared with that of SHR control animal. In line with this, endothelium-dependent relaxation was significantly improved in aortic ring of EGCG- and Losartan-treated SHR groups, respectively. In addition, cyclic guanosine monophosphate (cGMP) level was also significantly increased in isolated aorta tissue from SHR treated with EGCG and losartan respectively. In conclusion, this study shows that EGCG improves the vascular function of SHR which in part contributes to the decrease in blood pressure of the animals.

Keywords: Catechin, Vasoprotective, Blood pressure, Relaxation, cGMP

PCVS-02

REM sleep deprivation-induced endothelial dysfunction

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Oxidative stress is a known cause of endothelial dysfunction, an early sign of cardiovascular disease. Rapid eye movement (REM) sleep deprivation is associated with oxidative stress. To date, the pathogenesis of endothelial dysfunction following REM sleep deprivation remains poorly understood. This study aimed to investigate the effects of REM sleep deprivation on the descending thoracic aorta in the REM sleep-deprived rat model. Twenty-eight (28) male Sprague-Dawley (SD) rats were randomly divided into four groups: free-moving control rats (FMC), 72-h REM sleep-deprived rats (REMsd), tank control rats (TC), and 72-h REM sleep-deprived rats that pre-treated with daily vitamin C (RVC) at 100 mg/kg for four weeks. Rats were deprived of REM sleep using the inverted flowerpot technique. The descending thoracic aorta was isolated for *in vitro* functional study, oxidative stress markers measurement, and histology study using a scanning electron microscope. Systolic blood pressure (SBP) was significantly higher in the REMsd group compared to other groups. REMsd group showed impaired endothelium-dependent vasodilator responses to acetylcholine (ACh) compared to other groups. Levels of malondialdehyde (MDA) were significantly increased, whereas levels of total antioxidant capacity (TAC), superoxide dismutase (SOD) activity, and catalase (CAT) significantly decreased in REMsd compared to other groups. The endothelium of REMsd rat only showed features of endothelial damage. The increased levels of MDA are suggestive of lipid peroxidation in the blood

vessel, and oxidative stress may have triggered the process. Supplementation of vitamin C has beneficial effects against oxidative stress-induced endothelial dysfunction in REM sleep deprivation.

Keywords: Sleep deprivation, Endothelial dysfunction, Oxidative stress, Vitamin C

PCVS-03

MicroRNA profiling of human umbilical vein endothelial cells (HUVEC) exposed to hypertensive disorders of pregnancy using RNA Sequencing analysis

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Hypertensive disorders of pregnancy (HDP) have been shown to have significant effects on both mother and future offspring. Previous studies showed that in the short term, neonates of HDP have high risk to develop fetal hypoxia, premature birth, placental abruption and death *in utero*. Furthermore, offspring from hypertensive pregnancies display changes in endothelial function from early life and are at an increased risk of hypertension in adulthood. MicroRNAs (miRNAs) are non-coding single stranded RNA that can regulate gene expression at post-transcriptional or protein synthesis level during biological processes. However, to date, there is limited study on miRNA profiling of human umbilical vein endothelial cells (HUVEC) isolated from the offspring of patients with HDP. Therefore, this study aimed to compare the miRNA profile of HUVEC derived from the offspring of women with HDP and normotensive pregnancies using RNA sequencing analysis. Total RNA was isolated from HUVEC followed by RNA sequencing analysis. We identified 218 known miRNAs and 23 novel miRNAs that are significantly upregulated in HUVEC exposed to HDP. Of these, hsa-miR-196a-5p and hsa-miR-675-3p were remarkably upregulated by 9.6-fold ($P < 0.05$) and 23-fold ($P < 0.05$), respectively. These miRNAs target ST3GAL5/GM3 and GALNT10, which have been reported to be involved in angiogenesis and atherosclerosis. These preliminary results indicate that the hsa-miR-196a-5p and hsa-miR-675-3p

may have a regulatory effect on endothelial function of HUVEC exposed to hypertensive pregnancies. Thus, further study is required to validate the target genes and the function of hsa-miR-196a-5p and hsa-miR-675-3p in HUVEC exposed to HDP.

Keywords: Hypertensive disorders of pregnancy, microRNA, Human umbilical vein endothelial cells, RNA-sequencing, Offspring

PCVS-05

The mechanism of clozapine-induced cardiotoxicity on cardiomyocytes: A systematic review

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Clozapine is an antipsychotic effective for treatment-resistant schizophrenia. However, its use is limited secondary to severe adverse effects, including cardiomyopathy, myocarditis and arrhythmias. The review aimed to determine the clozapine's effects on isolated cardiomyocytes. Articles were retrieved from PubMed and EBSCOhost using keywords of "clozapine" AND "cardiomyocytes" from inception to June 2021. *In vitro* studies and English articles were included, while *in vivo* studies, review articles and articles in other language were excluded. Twenty-seven articles were retrieved initially. A final five articles were included in the qualitative analysis. Three studies utilized the rat ventricular cardiomyocytes, while the other two studies used isolated cardiomyocytes from atria or ventricle to determine the clozapine effects on voltage- and ligand-gated potassium channels. Significant reduction of both cardiomyocytes viability and reduced glutathione levels were reported in three studies. In contrast, there were remarkable increases in mitochondrial membrane potential collapse and disruption of lysosomal membrane integrity. The production of reactive oxygen species, malondialdehyde and oxidized glutathione, were significantly elevated compared to controls. Other than that, clozapine was reported to exert a significant inhibition on normalized tail currents in the rapid component of the delayed rectifier potassium current (Ikr). Another study reported significant inhibitions of clozapine on acetylcholine receptor-operated potassium current (Ik.Ach) induced and activated by carbachol and guano-sine 5'-[γ-thio] triphosphate, respectively, with higher concentration was required to inhibit the latter. The detrimental clozapine effects on cardiomyocytes were attributable to its ability to induce oxidative

stress, depletion of antioxidants, lysosomal and mitochondrial dysfunction, cell death and arrhythmias.

Keywords: Antipsychotic, Cardiomyocytes, Cardiotoxicity, Clozapine, Oxidative stress

PCVS-06

The role of miR-134-5p in 7-ketocholesterol-induced human aortic endothelial cell dysfunction

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Atherosclerosis causes arterial wall hardening and narrowing following plaque built-up and leads to coronary artery disease. Atherogenesis comprises of several sequential events and is initiated when low-density lipoproteins accumulate in the intima and leads to endothelial injury or dysfunction. Our previous study reported the deregulation of plasma circulating miR-134-5p in acute coronary syndrome patients but the role of miR-134-5p in endothelial dysfunction requires further investigations. Endothelial damage was induced by 7-ketocholesterol (7-KC) in human aortic endothelial cells (HAECs), whereby 7-KC is one of the most prominent oxysterols in atherosclerosis. HAECs cell growth inhibition was induced by 7-KC dose-dependently. Treatment with 7-KC at 20 µg/mL significantly up-regulated miR-134-5p, and induced the phosphorylation of AKT, whereas transfection with miR-134-5p hairpin inhibitor reversed the up-regulation of miR-134-5p and inhibited the phosphorylation of AKT. Inactivation of endothelial nitric oxide synthase (eNOS) indicates the induction of endothelial damage and 7-KC inhibited the phosphorylation of eNOS in the presence of A23187, the Ca^{2+} ionophore which was used to increase eNOS activation in HAECs. However, the inactivation of eNOS was attenuated by miR-134-5p hairpin inhibitor in HAECs. In addition, 7-KC also increased the expression of adhesion protein E-selectin and down-regulated the tight junction protein VE-cadherin which indicate the disruption of endothelial barrier in HAECs. The deregulation of VE-cadherin was reversed by transfection of HAECs with miR-134-5p inhibitor. Collectively, these findings suggest that miR-134-5p is involved in the induction of endothelial dysfunction following 7-KC treatment in HAECs.

Keywords: Endothelial dysfunction, HAECs, miR-134-5p, 7-ketocholesterol, Atherogenesis

PCVS-07

Haplotype and diplotype association of human aldosterone synthase (*CYP11B2*) gene polymorphisms to essential hypertension in Malay peninsular Malaysia

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Essential Hypertension (HT) is a complex progressive cardiovascular disorder, primarily driven by Renin-angiotensin-aldosterone system (RAAS). The last step of RAAS involves the aldosterone (ALDO) biosynthesis by enzyme aldosterone synthase, encoded by the gene *CYP11B2*. *CYP11B2*-rs1799998 and rs10087214 have been reported to be associated with HT, however they are not adequately studied in the Malays. This study aims to investigate association between *CYP11B2* and HT. A total of 918 individuals (500 HT and 418 normotensives, NT) were recruited and genotypes were determined. Genetic association study analysis was determined using Fisher exact test and statistically adjusted with logistic regression; while Independent T-test was performed to examine the association between the risk variants and alteration of BP. Genetic association revealed a significant association between HT and *CYP11B2* variants; rs1799998 (p = 0.028) and rs10087214 (p = 0.027). Further investigation revealed male HT carrier for haplotype, G-A had higher BP than the non-haplotype carriers (pSBP = 0.015 pDBP = 0.047 and pMAP = 0.029). Similar finding was observed in diplotype, GG-AA (pDBP = 0.025 and pMAP = 0.018). In contrast, the female HT carrier for haplotype, G-A had lower BP than the non-haplotype carriers (pSBP < 0.001). The *CYP11B2*-rs1799998 and rs10087214 are associated with significant elevation of BP among HT Malay.

If proven to be true, this SNP could potentially be applied as a potential pharmacogenetic marker for HT treatment.

Keywords: Hypertension, Haplotype, Diplotype, *CYP11B2*, Pharmacogenetic.

OMECP-03

Disposal practices of unused medication among pharmacists in Libya

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For the past decade, disposing of unused drugs has become a source of concerns globally; as pharmaceutical waste enters the ecosystem, posing a threat to human health and the environment. This study aimed to assess the disposal practice of unused medicine among pharmacists in Libya. This study also seeks to determine if pharmacists plan to have their pharmacies serve as collection points for potential take-back initiatives. A random sample of 150 pharmacists from various public and private pharmacies in Tripoli participated in a self-administered questionnaire about their disposal practices, and their knowledge on the ideal disposal methods of unused medicines. The outcome is supported by statistical data used to analyze the out findings. A total of 128 pharmacists completed the survey. Throwing unused medicines in the trash was the main method of disposal by a majority of the respondents (53.1%), followed by discarding via burn and drug wholesalers (17.2%, 14.8%, respectively). Only 2.1% of the respondents disposed of unused medicines according to the WHO guidelines of drug disposal. Moreover, about 65.6% had poor knowledge about the Take-Back program. Failure to follow the WHO guidelines for drug disposal raises the risk of contamination of our environment and the likelihood of humans and animals ingesting harmful pharmaceutical wastes.

Keywords: Take-back Program, Prescription Disposal, Pharmacist Awareness

OMECP-04

Acceptance of covid-19 vaccine among general population of South India – A cross-sectional survey

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COVID-19 vaccines provide concrete hope of mitigating the spread of the virus and enabling countries worldwide to resume financial and social activities disrupted by the pandemic. Several COVID 19 vaccines have already received approval from regulatory bodies across the world, the vaccine rollout has started and many countries are implementing mass vaccination campaigns. This study aims to evaluate the acceptability of COVID-19 vaccines and its predictors, along with the attitudes towards the vaccines among the general population of South India. This study was conducted as an online survey during December 2020 and January 2021. Excel 2019 and SPPS 24 were used for statistical analysis. Descriptive statistics were used, and a Chi-square test was performed. A total of 686 people has participated in this study, with a mean age of 30.4 years. 30.9% of study participants have already been infected with COVID-19. 76.2% responded '*yes*' for accepting the COVID-19 vaccine, 69% responded to prefer '*routine*' administration of the vaccine, and 50.1% were likely to take the COVID-19 vaccine '*as soon as possible*' once available. Public health authorities and policymakers need to streamline systematic interventions and awareness campaigns to improve the acceptance of COVID 19 vaccines and reduce vaccine hesitancy levels. Vaccination strategy should be targeted at the specific needs and attitudes of the concerned population. Reviving the trust in the vaccination procedures

and outcomes and offering transparent information regarding the vaccines' efficacy and safety seem to be particularly importance for the population of our study.

Keywords: Acceptance, COVID-19, Vaccines, India, Vaccination, Pandemic, SARS-CoV-2

OMECP-09

Investigation of the association between genetic polymorphisms and cholesterol-lowering effect of statin among outpatient statin users in hospital USM

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Inter-individual variability of statin in lowering cholesterol levels varies due to several factors including genetic polymorphisms. Single nucleotide polymorphisms (SNP) in CETP rs708272, ABCG2 rs2231142, ABCC2 rs717620, GATM rs9806699, COQ2 rs4693075, APOA5 rs662799 and APOE gene have been associated with statin efficacy. This study aimed to investigate the association between the indicated SNPs and cholesterol-lowering efficacy of statin among hypercholesterolaemic statin users in Hospital USM. In this cross-sectional study, 229 hypercholesterolaemic patients were genotyped using PCR-RFLP method. Lipid profiles were compared between minor allele carriers and non-carriers using a recessive model after approximately 7 months of treatment. Minor allele carriers of ABCC2 rs717620 (2.17 $\pm$ 1.14 mmol/L vs. 1.48 $\pm$ 0.75 mmol/L, P=0.009) and APOA5 rs662799 (1.64 $\pm$ 0.58 mmol/L vs. 1.57 $\pm$ 0.97 mmol/L, P=0.037) had lower triglyceride levels. Minor allele carriers in APOA5 rs662799 also had higher HDL-c (1.19 $\pm$ 0.20 mmol/L vs 1.27 $\pm$ 0.25 mmol/L, P= 0.031). In contrast, there was an association of minor allele carriers of ABCG2 rs2231142 with higher total cholesterol levels (4.85 $\pm$ 1.04 mmol/L vs. 5.13 $\pm$ 1.23 mmol/L, P=0.038) after 7 months treatment. Other SNPs including SNP in the APOE gene, were not significantly associated with statin's cholesterol-lowering effects. In conclusion, ABCC2 and APOA5 could be promising drug targets and novel markers for drug discovery to revolutionize the treatment of hypercholesterolaemia.

Keywords: Statin, Hypercholesterolaemia, Genetic polymorphism, ABCC2, APOA5, APOE

OMECP-11

Physical activity and emotional intelligence: Finding the relationship amongst the university students in Malaysia

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Physical activity (PA) is an indifferent part of wellbeing. PA develops emotions, improves cognition, reduces anxiety, improves sleep, and prevents mental health-related diseases. Emotional intelligence (EI) is strongly associated with health and psychological benefits. There is sparse information about the relationships between PA and EI amongst students in Malaysia. The aim of this study was to investigate the relationship between PA and EI of undergraduate students. A total of 149 (20.89 $\pm$ 1.94 years) undergraduate students (male 53, female 96) completed the Global Physical Activity Questionnaire for PA levels, Trait Meta-Mood Scale for EI measurement and a sociodemographic questionnaire. Spearman's correlation analysis was used to determine the relationship between EI components and PA (significance level, $p < 0.05$). We observed mood repair (a component of EI) was significantly associated ($p < 0.05$) with physical activity with a spearman's rho of 0.172 and overall EI was significantly associated ($p < 0.05$) with physical activity with a spearman's rho of 0.171. Females scored significantly higher ($p < 0.05$) in the attention to feelings component of EI as compared to males. As conclusion, it was suggested that physical activity boosts mental health which is reflected as an improvement of emotional intelligence in this study. Findings of this study will help to implement and improve best health practices and policy especially in higher education sectors.

Keywords: Emotional intelligence, Health, Physical activity, Students, University

OMECP-12

Over-the-counter medicine attitudes and knowledge among university and college students in Brunei Darussalam: Findings from the first national survey

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Being primary social media users, university and college students are more likely to be exposed to unverified sources of health information. This study was aimed to determine the knowledge, attitude, and practice of over the counter (OTC) medicine among higher institution students in Brunei Darussalam. A cross-sectional study was performed using a self-administered online questionnaire, adapted from the literature with additional information from the United States Food and Drug Administration on the educational resources in understanding OTC medicine for consumers. Ethics approval was granted by the university ethics committee. The questionnaire consisted of four sections: demographic information, knowledge on OTC, attitude, and practice. Descriptive and appropriate inferential statistics were used for data analysis. A total of 335 respondents completed the survey, giving a response rate of 63.8%. The median age of the respondents was 22.0 years (standard deviation=3.0, range between 18 and 44 years). More than half of the respondents showed a good level of knowledge on OTC, with a mean total knowledge score of 7.1 out of 9. Chi-square tests showed that the students' level of knowledge was significantly different in terms of gender ($P=0.01$) and the course of study ($P<0.01$). Moreover, the Fisher exact test revealed that the respondents' level of knowledge was quite different in terms of academic degree ($P=0.01$), but not in terms of nationality and year of the study. Even though good level of knowledge was reported, the risky practice of certain

respondents, especially the recommended dose and the adverse effects aspect of OTC should be rectified.

Keywords: Non-poison, Non-prescribed medication, Cross-sectional survey, Medication Safety, Knowledge, Attitude, Practice

OMECP-13

Educational and psychological impact of COVID-19 and lockdown among university medical students in Mauritius

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The primary objectives of the study were to find the educational and psychological impact of lockdown on medical students due to COVID-19. A cross-sectional study was conducted at Sir Seewoosagur Ramgoolam Medical College, Mauritius from May-June 2020. A validated questionnaire was used to collect the sample through Google form. The internal consistency between the items using Cronbach's alpha was found to be 0.717. A total of 663 students out of 700 participated in the study, which gives an overall response rate of 95%. Due to the pandemic, 348 (52.5 %) of the students were stationed in their hometown and 315 (47.5 %) were stationed in Mauritius. 634 (95.6%) students suffered from the educational impact and 464 (70%) students suffered from the psychological impact due to lockdown. Mauritian students suffered from a greater educational impact aOR 4.236 [1.606-11.173]. Students pursuing clinical studies has aOR 1.219 [0.531-2.798] educational impact as compared to preclinical studies. Lockdown triggered both educational and psychological impact on medical students. On a psychological basis it was proven that the lockdown induced a feeling of guilt and had subsequent psychological impacts in certain students. The COVID-19 situation was simultaneously indicated to be a motivator in the majority of students; however, juxtaposed to this was the fact that various students felt as if they could not study at the same level that they are accustomed to due to the uncertainty of the situation.

Keywords: Anthropology, Education, Geographical Locations Category, Public Health, SARS-CoV-2

OMECP-16

Alginate micro-beads prepared by dripping/ electrospraying methods: A comparative study

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Calcium-alginate hydrogel particles are attracting high attention from scientific community due to their important applications as carriers for bioactive molecules. Investigating and enhancing the mechanical properties of hydrogel particles is critical to avoid difficulties in manufacturing process and limitations associated with the final product. Electrospraying is one of the novel techniques that able to produce a wide range of particle size. Its principle relies on formation of small droplets by applying voltage to polymeric solution that pumped through a thin metal needle. Compared with the dripping method, electrospraying has potential to generate monodisperse droplets in the range of nano- to micrometer using low amount of solvents and high yield. Solid micro-beads were manufactured by dripping and electrospraying methods. This work examines the effects of dripping method parameters, alginate concentration, $CaCl_2$ concentration, and needle gauge, on the size, aspect ratio, sphericity, water uptake, swelling and erosion of the particles. Furthermore, the influence of applied voltage on the same responses was also studied to compare between both methods. The results indicate that alginate concentration, $CaCl_2$ concentration and needle gauge have a strong influence on the response variables. Spherical beads with high percentage of erosion and small diameters as well as low percentage of water uptake and swelling were obtained by decreasing alginate concentration, needle gauge and increasing $CaCl_2$ concentration. While, applying voltage causes a decrease in particles size and percentage of erosion as well as improved particle's sphericity and increased the percentage of water uptake and swelling of the particles.

Keywords: Alginate, Micro-beads, Electrospray, dripping, Ionic gelation, Water uptake, Erosion

OMECP-18

Evaluation of drug-drug interactions among pediatrics in tertiary care hospital: Findings from Pakistan

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The aim of this investigation was to identify the drug-drug interactions in hospitalized pediatric patients associated with polypharmacy, to identify patients and practices at increased risk of potential drug interactions and to categorize the drug interactions according to severity and as pharmacokinetic or pharmacodynamic interactions. This study was a cross-sectional, prospective analytical study performed at pediatric tertiary care hospital in Lahore, Pakistan for the duration of 4 months which included 300 patients' prescription orders. Data was collected from patient medical files about previous and current medication history. Drug interactions were analyzed using interaction checker on Medscape and categorized according to the severity levels. Out of 300 patients, the occurrence of drug interactions was found among 157 (52.3%) patients while in 143 (47.7%) patients, no interaction was found. Among these interactions, 50.70% were pharmacodynamic interactions and 49.30% were pharmacokinetic interactions. 81% prescription orders with drug interactions contained more than 3 drugs and 11.9% interactions were severe. Majority of interactions were of Amikacin-vancomycin, Piroxicam-captopril and captopril-ciprofloxacin. In conclusion, majority interactions were of moderate nature and among those patients, they were prescribed with multiple drugs. The drug interactions can be minimized by providing special patient monitoring and adequate management with prior knowledge of these drug interaction.

Keywords: Drug-drug interaction, Pediatrics, Cross-sectional study

OMECP-19

Dengue fever and building constructors in Klang Valley Malaysia

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Construction sites have frequently been reported as dengue hotspots due to poor work planning and execution, and the constructors are often to blame. The spread of viruses into surrounding areas suggested that construction sites are an important driver of long-term dengue transmission. Nonetheless, little is known about what constructors know about dengue fever and how they prevent the disease from spreading on construction sites. This study investigated the knowledge of dengue and dengue prevention practices of building constructors in Klang Valley, Malaysia. Mean ranking analysis and factor analysis were performed on quantitative data collected from 123 respondents via a questionnaire survey. The main findings of the knowledge of dengue revealed that building constructors were aware that 'periodically emptying or drying out containers can prevent mosquitoes breeding', 'proper disposal of unwanted items capable of retaining water around the site can prevent mosquitoes breeding', and 'dengue haemorrhagic fever can be fatal'. Important dengue prevention practices used by building constructors included 'properly disposing the waste from site', 'cleaning up the site area', and 'clearing out debris that may block water flow in drain or roof gutter'. The underlying knowledge of dengue was found to be related to awareness and attitudes, medical facts, dengue virology, occurrence factors, dengue entomology, and dengue control whereas the underlying dengue prevention practices were found related to prevention of mosquito bites, source reduction practice, prevention of dengue transmission, and prevention of mosquito breeding.

Future research can build on this study to educate building constructors about dengue and dengue prevention.

Keywords: Dengue fever, Knowledge of dengue, Dengue prevention practices, Building constructors, Klang Valley Malaysia

PMECP-01

Investigating the expression of endometrial receptivity markers in women with polycystic ovary syndrome following progesterone therapy

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Polycystic ovary syndrome (PCOS) in women is associated with a high prevalence of implantation failure due to abnormal endometrial function. Expression of the endometrial receptivity markers including αvβ3 integrin, Hb-EGF, Mucin-1, and E-cadherin during implantation window has been used to predict successful embryo implantation. Thus, this study aimed to investigate the expression of endometrial receptivity markers in PCOS women following progesterone therapy. A total of 40 women aged 26 to 45 were divided into two groups: PCOS (n=20) and normal control (n=20) groups. In the PCOS group, daily oral micronized progesterone (Utrogestan 200mg) was administered for ten days, while the control group was monitored for normal regular menses and ovulation. Blood and endometrial tissue biopsy (using Pipelle de Cornier catheter) were collected in all groups. The endometrial biopsy was collected during the mid-secretory phase, which occurred 7-9 days after ovulation. The serum hormone levels were determined using ELISA, and the genes expression was quantified using quantitative PCR. We found that FSH, oestradiol, and progesterone levels were statistically lower in the PCOS group than in the control group ($p<0.05$). Meanwhile, LH and DHEA levels of the PCOS group were not statistically different from the control group. Besides that, no significant changes were found in the endometrial αvβ3 integrin, Hb-EGF, Mucin-1, and E-cadherin expression in both groups. In conclusion, endometrial Hb-EGF, αvβ3 Integrin, Mucin-1, and E-Cadherin

expression does not differ between PCOS and normal women, suggesting further study to discover the relation of these genes to PCOS women.

Keywords: Progesterone, Anovulatory, Endometrial receptivity markers, Implantation failure, Infertility, Implantation window

PMECP-03

To improve engagement and understanding of cardiac cycle in teaching and learning: A novel education method using augmented reality

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Augmented Reality (AR) for Cardiac Cycle (CC) through mobile devices (i.e., mobile phone and tablet) is one of a novel method for revolution of physiology teaching and learning (T&L) in Malaysia among educator and learner (E&L). AR refers to a real time pictorial technique that overlays a computer-generated image on a user's view of the authentic world. This 3D technique will allow E&L to learn and assess their CC knowledge effectively as compared to traditional learning method. The complexity and dynamic nature of T&L in CC teaching need a clear and precise visualisation to deliver the subject effectively. During Covid-19 pandemic, the access of E&L to traditional face to face method of T&L is very limited. This traditional method usually adapts the normal two-dimension (2D) sources including medical books, lecture notes, white boards and internet websites. The development of the CC AR is based on normal cardiac anatomy and physiology. The method involving image modelling, mapping, texturing, animation and rigging. The AR programming utilised Unity 2017.3.1, a software to develop AR. Adobe Illustrator CS6 was used to create the design for user friendly interface for this application. The three-dimension (3D) AR method had been showed in other study to be advantageous as this can help both E&L for T&L in cardiac cycle via 3D approach. It is proposed that this method may increase engagement and improve understanding of cardiac cycle concept effectively.

Keywords: Cardiac cycle, Heart, Anatomy, Physiology, Augmented reality, E-learning

PMECP-04

Elucidating the use of biointerfaces as a nanovehicle as a dual drug delivery strategy against Methicillin-Resistant *Staphylococcus Aureus* (MRSA)

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The key element that will be used to construct the phospholipid bilayer of the 'stealth' liposomes is a mixture of egg yolk phosphatidylcholine (EPC), cholesterol, and mPEG2000. DAPT-PEG-DSPE, which is produced by an amide reaction between daptomycin and NHS-PEG, will be combined with the other three components and act as a targeting ligand. Using I-optimal (combined) with two-factor at five levels, the high-energy ultrasonication processing method was improved. On the development of nanoliposomal carriers, the effects of ultrasonic intensity (A), sonication time (B), and component mixture were examined. The aforementioned elements, particularly the sonication period (B), has a massive effect on the polydispersity index value. With a 78.038% ultrasonic intensity and a sonication time of 9.019 minutes, nanoliposomes of a desirable size can be generated. The average size of the particles was 108.13 $\pm$ 1.16 nm, with a polydispersity index of 0.205 $\pm$ 0.10. The improved formulation had an encapsulation efficiency of 45.36

± 4.17 for vancomycin liposomes (VAN-L) and 90.53 ± 3.90 for daptomycin coupled liposomes (DAPT-L). Encapsulation efficiency was 39.76 ± 6.17 (VAN-L) and 86.65 ± 6.13 (VAN-L) when using RBC membrane and a dual drug combination (DAPT-L). The stability study of blank liposomes and RBC coated daptomycin and vancomycin liposomes (RBCDVL) revealed certain physicochemical variations, such as withering of the natural biomarker on the surface of the formulation by SDS PAGE and aggregation by TEM on 14 days above, but also revealed good antibacterial activity against MRSA and less cytotoxicity in in-vitro and in-vivo studies.

Keywords: Erythrocytes, Dual drug delivery, Liposomes, MRSA, Vancomycin, Daptomycin

PMECP-06

Correlation of height and BMI with motor nerve conduction parameters in both arms of young adults

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This study aimed to establish the normal electrophysiology of both median and ulnar nerves, and their correlation with height and BMI in both arms among healthy young adults. Nerve conduction studies were performed prospectively in the upper limbs of 60 carefully screened healthy individuals, aged between 19 and 21 years, using a standardized technique. The study showed that the proximal latencies and peak amplitudes of median and ulnar nerves of the right arm were 7.0 $\pm$ 0.7ms vs. 6.9 $\pm$ 0.7ms and 4.4 $\pm$ 2.7mV vs. 4.7 $\pm$ 2.9mV, respectively. The conduction velocity of median and ulnar nerves were comparable on the right arm (53.6 $\pm$ 8.0 m/s vs. 53.7 $\pm$ 7.7 m/s). On the left arm, proximal latencies of both nerves were shorter, but the peak amplitudes and the conduction velocities (Median vs. ulnar nerves: 55.4 $\pm$ 12.4 m/s vs. 59.7 $\pm$ 7.9 m/s) were higher as compared to the other side. On the right arm, both height and BMI were significantly correlated with proximal latency of median nerve, whereas ulnar nerve showed a significant correlation with height only ($p<0.05$). Similarly, the conduction velocities of both nerves correlated positively with BMI and height only in the right arm. Also, a significant difference ($p<0.01$) in conduction velocity of the ulnar nerve was noted in both arms. In conclusion, height and BMI influenced both proximal latency and conduction velocity of the median nerve, but only the conduction velocity of the ulnar nerve on the right arm.

Keywords: Latency, Amplitude, Velocity, Ulnar, Median, Upper limb

PMECP-07

Comparison of computer-based Ishihara test versus online D-15 dichotomous test in colour vision screening

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Most online colour vision tests have varying degrees of quality and are variations of classical Ishihara test. The choice of test depends on multiple factors, including the reason for assessment of the persons, however, it is necessary to choose quick and accurate screening test in clinical practice. Objective of this study is to compare the computer-based Ishihara test and online D-15 dichotomous test in colour vision screening. A total of 302 medical and nursing students aged between 17-25 years were screened by these two tests in a computer lab in University Malaysia Sarawak. The results showed 295 (97.7%) normal and 7 (2.3%) defects in Ishihara test; while 292 (96.7%) normal and 10 (3.3%) defects in the online dichotomous test. Of 70 males and 232 females, 7 (10.0%) males in the Ishihara test, 8 (11.4%) males, and 2 (0.9%) females in the online test were found to have defects. There was strong agreement between results of two tests (Kappa:0.82). In this study, Ishihara test screens the colour vision and dichotomous test shows the type and severity of the vision defect, which mainly occurs in male. This present study concludes that a standardised online colour vision test is equally comparable to the traditional Ishihara test, thus providing an alternate robust option for colour vision screening in healthcare practice. Nevertheless, any person identified as colour vision deficient by online screening tools will require to further consult with an eye care professional.

Keywords: Colour vision, Accurate & robust, Screening test, Computer-based Ishihara test, Online D-15 dichotomous test

PMECP-09

Systematic review of pneumococcal infection, diagnosis, and treatment in Malaysia

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In Malaysia, pneumococcal infection has been a significant burden. The emergence of antimicrobial resistance has been life-threatening. Several studies assess the cost-effectiveness of pneumococcal vaccination. However, various aspects of pneumococcal diseases remain scarce due to the lack of robust evidence. Although several associated studies have been held, there is an urgent need to establish collected documentation of the individual findings. In this article, significant aspects discussed include the prevalence of pneumococcal serotypes, antimicrobial susceptibilities, specific serotypes linked to antimicrobial susceptibilities, molecular and genotypic characterization associated with antimicrobial susceptibilities, and also the coverage and impacts of pneumococcal vaccinations. Online searches were conducted via PubMed and Scopus from 2000 up to 2021, which returned 129 studies. After the screening of abstracts, 38 studies were shortlisted, and data extraction was conducted for 26 studies following full-text screening. Most of the findings have shown the prevalence of serotypes 19F, 23F, 6A/6B, and 19F. A significant association was found between serotype and penicillin susceptibility (p<0.001). Most of the penicillin-resistant isolates were of serotypes 19F, 23F, 6A, and 6B. This suggests that pneumococcal serotypes are closely linked to antimicrobial susceptibilities. Antimicrobial resistance was closely associated with *pbp*, *erm*(B), and *mef*(A) genes. Majority of the studies reported an estimated vaccination coverage of over 50%. PCV13 was estimated to imply more significant impacts, resulting in higher cost-effectiveness than PCV7

and PCV10. These findings emphasise the need for continuous surveillance of pneumococcal diseases, a revised national vaccination policy, and a database for diagnosing pneumococcal diseases in Malaysia.

Keywords: *Streptococcus pneumoniae*, Pneumococcal infection, Serotype, Antibiotic, Antimicrobial susceptibility, Molecular characterisation, Genotypic characterisation, Pneumococcal vaccine

PMECP-10

Knowledge, attitude, and practice of clinicians about antimicrobial stewardship and resistance among hospitals of Pakistan: A multicenter cross-sectional study

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Considering that antimicrobial resistance (AMR) is a global challenge, there is a dire need to gauge the knowledge, attitude, and practice (KAP) of clinicians in endemic countries. The aim of the current multicenter, cross-sectional study was to highlight the knowledge, aptitude and practice gaps in antimicrobial (AM) stewardship and AMR among practicing doctors working in public tertiary care teaching hospitals of Lahore, Pakistan. A KAP survey, based on a self-administered questionnaire containing 45 questions, was conducted among 336 clinicians practicing in 6 randomly selected hospitals of Lahore, Pakistan. Overall, 92% of the clinicians considered AMR as a worldwide problem but only 66% disagreed that cold and flu symptoms require antibiotics. Moreover, around 68% doctors felt confident about their practice in AM but still 96% felt need to get more knowledge about AM. Need to establish courses on rational antibiotic use was demanded by 84% of participants. The main contributing factors considered for AMR by the doctors included excessive AM usage in medical profession (87.1%) and multiple antibiotics per prescription (76.4%). Pharmacologically, AM spectrum was accurately chosen by 1.4% (ampicillin), 0.003% (erythromycin) and 0% (levofloxacin).

Clinically, a more than 50% of clinicians used miscellaneous AM for empirical therapy of respiratory tract infection and cholecystitis. The data was analyzed using Statistical Package for Social Sciences (SPSS) version 25. The knowledge of clinicians is relatively poor in AM spectrum and drugs of choice for certain infections. However, they know about their short comings with positive approach towards improvement.

Keywords: Antimicrobials, Antimicrobial resistance, Antimicrobial use, Antibiotic misuse, Antibiotic resistance, KAP survey

PMECP-12

Internet gaming disorder: Prevalence and effects on insomnia and psychological distress among young adult gamers in Malaysia

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Nowadays, internet gaming has become popular activities among young adults to fill their empty times during COVID-19 pandemic period. Internet games is beneficial when played in moderation. It can improve critical thinking skills, problem solving skills and moods. However, excessive internet gaming can develop internet gaming disorder (IGD), which also can lead to other health problems such as sleep problems and psychological distress. The aim of this study was to determine the prevalence of IGD and its association with insomnia and psychological distress (depression, anxiety, and stress) among young adult gamers in Malaysia. A cross-sectional study comprising Malaysian young adult gamers (N=271) aged 18 to 24 years was conducted from January 2021 until May 2021. Three validated questionnaires were used to assess the internet gaming disorder, insomnia, depression, anxiety and stress: Internet Gaming Disorder Scale-Short Form (IGDS9-SF), Athens Insomnia Scales (AIS), and Depression, Anxiety, Stress Scales–21 (DASS-21). Result showed that the prevalence of IGD among young adult gamers in Malaysia was 3.6%. There was significant association between IGD and insomnia, depression, anxiety and stress. In conclusion, the prevalence of IGD among young adult gamers in Malaysia is considered low. However, IGD must be given attention by healthcare provider and publics to avoid this disorder become worse and effect their physical and mental wellbeing.

Keywords: Internet gaming disorder, Prevalence, Insomnia, Depression, Anxiety, Stress

PMECP-13

Model making: Unveiling the art in medicine

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This paper presents the perceptions of model-making by medical students undergoing an integrated curriculum. The theme for the models were based on the learning outcomes in year one taught in six blocks. The aim is to find out the perceptions of students on their model-making experience and the effectiveness of the student-centred learning activities. The purpose of model-making was explained to the students and they consented to participate in the study. 136 students were enrolled and divided into 12 groups. Students drew lots to assign themselves the blocks and the theme of the models were chosen by the student groups. After 3 weeks, the students exhibited their models, presented the concepts and assessed by subject experts. A questionnaire survey was administered to elicit the perceptions of the students. The student groups were given constructive feedback and rewarded with prizes upon presentation. Descriptive statistics was used to analyse the data. Results revealed that 86% of the students found the activity interesting, 77% agreed it helped cover the learning outcomes, 74% thoroughly enjoyed performing the activity, 76% felt it enabled peer learning and 72% said that they understood and remembered concepts better after the activity.11% did not find it useful and 10% opined that it wasted their time. In conclusion, majority of the students enjoyed the model-making activities, found it interesting, agreed that it helped cover learning outcomes, reinforced their knowledge of concepts and facilitated peer learning.

Keywords: Model making, Project, Medical students, Perceptions, Art and medicine

PMECP-14

Influence of knowledge and attitude in quality of life type 2 diabetes mellitus patients from private specialist hospitals in Malaysia

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The study aims to evaluate the influence of knowledge and attitude towards the quality of life (QoL) of patients type 2 diabetes mellitus (T2DM) in private hospitals in Malaysia. A cross sectional survey of the knowledge, attitude and QoL towards the patient with T2DM in two private hospitals were carried out from February to June 2020. The study was conducted using a validated questionnaire comprises of three sections: Socio demographic, assessment of the knowledge and attitude toward diabetes, and identification of the QoL of the patient with T2DM. A total of 80 patients with T2DM, mean age of 59.4$\pm$10.86 years old, participated in this study. Majority (95%) of patient had good score of knowledge and only 5% had poor knowledge. 70% patients were with good attitude and 30% with low attitude. Male participants have significantly poorer attitude towards diabetes management compared to female participants ($p=0.014$). While 47.5 % of patients had use insulin presently. 84.2% of patients do not double up the dose in the situation of missing dose. And 58.8% patient had good score in QoL and 41.3% moderate score QoL. There was no significant association of the patient knowledge and attitude toward diabetes with QoL ($p=0.1$) and ($p=0.143$) respectively. This study concluded there was no association of knowledge and attitude with QoL of T2DM. This research may be useful for optimizing diabetic care commitment preparation approaches as maintaining high QoL score as well as minimizing the morbidity and mortality rate of chronic disease.

Keywords: Quality of Life (QoL), type 2 Diabetes Mellitus (T2DM), Knowledge, Attitude, Private hospital

PMECP-15

Systematic review on methods of assay for modified release metformin tablets

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Metformin is one of the most popular prescribed anti-diabetic drugs. We performed a systematic review on the various methods of assay for metformin modified release tablets by using various instrument. Studies were search using PubMed, Science Direct and Google Scholar. Combinations of the following terms: metformin, extended-release, assay, pharmaceutical analysis, HPLC and spectrophotometry was used. Inclusion criteria were studies that mentioned the current assay method in analysing metformin extended-release tablets. Exclusion criteria were studies that adopted other identification test result to replace assay method in proving the safety, efficacy and quality of metformin XR tablet. The search resulted in a total of 75 records (39 from PubMed, 26 from Science Direct, 10 from Google Scholar). After screening, 23 articles met the inclusion criteria and were further examined with the full-text report. Eventually, total of 10 studies were included in this systematic review. Study conducted by Huang et al. (2006) and Umapathi et al. (2012) believed that the interaction between metformin and excipients resulted variation in the accuracy and consistency of the result and thus problem resolved by reducing and inhibiting the presence of drug-excipient interactions. Methods using ethanol and methanol as the substitution of water in sample preparation was found to be suitable for general metformin XR formulations. On the other hand, method using arginine as a competitor to form complex with croscarmellose in order to let metformin freely bound and increase its recovery percentage during pharmaceutical procedure is suitable for formulations containing croscarmellose sodium.

Keywords: Assay, Pharmaceutical Analysis, HPLC, Chromatography, UV-vis spectrophotometry

PMECP-20

Effectiveness of pharmacological intervention among men with infertility: A systematic review and network meta-analysis

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Infertility among men is an emerging health issue. The aim of this review is to investigate the efficacy of various pharmacological interventions among men with idiopathic male infertility. All randomized control trials evaluating the effectuality of interventions on male infertility were included for NMA from inception to 31st April 2020 systematically performed using STATA through random effect model. The protocol was registered at PROSPERO (CRD42020152891). The outcomes of interest were semen and hormonal parameters. Treatment effects ($p < 0.05$) were estimated through WMD at the confidence interval of 95%. Upon applying exclusion criteria, n=28 RCTs were found eligible for NMA. Results from NMA indicated that consumption of supplements increase sperm concentration levels [6.26, 95% CI 3.32, 9.21] in comparison to SERMs [4.97, 95% CI 1.61, 8.32], hormones [4.14, 95% CI 1.83, 6.46], vitamins [0.15, 95% CI -20.86, 21.15)] with placebo, whereas, the use of SERMs increased percentage sperm motility [6.69, 95% CI 2.38, 10.99] in comparison to supplements [6.46, 95% CI 2.57, 10.06], hormones [3.47, 95% CI 0.40, 6.54] and vitamins [-1.24, 95% CI -11.84, 9.43] with placebo. Consumption of hormones increased the sperm morphology [3.71, 95% CI, 1.34, 6.07] in contrast to supplements [2.22, 95% CI 0.12, 4.55], SERMs [2.21, 95% CI -0.78, 5.20] and vitamins [0.51, 95% CI -3.60, 4.62] with placebo. Supplements boosted the total testosterone levels [2.70, 95% CI 1.34, 4.07] in comparison

to SERMs [1.83, 95% CI 1.16, 2.50], hormones [0.40, 95% CI -0.49, 1.29] and vitamins [-0.70, 95% CI -6.71, 5.31] with placebo. SERMs increase the serum FSH levels [3.63, 95% CI 1.48, 5.79] better than hormones [1.29, 95% CI -0.79, 3.36], vitamins [0.03, 95% CI -2.69, 2.76] and supplements [-4.45, 95% CI -7.15, -1.76] in comparison with placebo. This review establishes that all interventions had a significantly positive effect on male infertility. Statistically, significant increase of sperm parameters were noted in combination of zinc sulphate (220mg BID), clomiphene citrate (50mg BID) and testosterone undecanoate and CoQ10, tamoxifen citrate and FSH were shown to improve hormonal profile in infertile males.

Keywords: Male infertility, Meta-analysis, Network meta-analysis, Weighted mean difference, Selective estrogen receptor modulator, Co-enzyme Q10, Follicle stimulating hormone

PMECP-21

Effect of vitamin E and vitamin C supplementation on antioxidant enzymes in down syndrome individuals

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The Cu-Zn superoxide dismutase (SOD) gene is present on chromosome 21, thus, individuals with Down syndrome (DS) may be under oxidative stress. Antioxidants supplementations are thought to decrease the oxidative stress level. Therefore, the objective of this study was to determine the effects of Tocotrienol Rich Fraction (TRF) and vitamin C supplementation on antioxidant enzymes in Down syndrome individuals. Sixty individuals (aged between 2 to 29 years old) with Down syndrome were recruited and randomly assigned to receive either supplementation (n=30) with TRF (150 mg) and vitamin C (250 mg) or placebo (n=30). Blood samples were obtained from each subject at 0, 3rd and 6th months for the measurement of antioxidant enzymes i.e. superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx). Changes in the activities of antioxidant enzymes with TRF and vitamin C were not observed when comparing the baseline to 3 and 6 months for SOD activity as well as in CAT and GPx ($p>0.005$). There were no association between SOD, CAT and GPx activities and age in both treatment and control groups ($p>0.005$). In summary, it can be concluded that there was no significant difference in the levels of antioxidant enzymes and further study should be conducted in order to understand the mechanism/s that contributed to this condition.

Keywords: Down syndrome, TRF, Vitamin C, Antioxidant, Oxidative stress

PMECP-22

An investigation into awareness and utilization of emotional intelligence in Pakistani universities

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Emotional intelligence is the ability to express feelings and emotions, to use according to the situation. The study's objectives were to identify how much university students are aware of their emotions and how they assume other's emotions. The research was quantitative by nature; the study population was all HEC ranked University in the premise of Punjab. Eleven Universities were selected as samples through stratified sampling technique; 359 students from all universities were selected using convenience sampling. An international tool named "Levels of Emotional Awareness Scale (LEAS)" was adopted and translated for data collection. LEAS measure consists of 20 scenarios, but in this study, the researcher uses 10 scenarios selected with the help of a pilot study based on the most responsive statements/scenarios. The final tool was bi-lingual, which was used for data collection. Data were collected by personal visits, with proper channels and permission from all selected universities. Firstly, answers to the respondents' open-ended questions were coded according to the guidelines of LEAS measure (quantify the qualitative data). Final data were analyzed through (SPSS ver. 24), Independent Sample t-test, One-way ANOVA, and Pearson coefficient correlation was applied. The study results show a weak significance difference between the emotional intelligence of Employed and unemployed, but Employed students perform well academically. Female students perform well academically (CGPA) and are more emotionally aware. Based on Education/degree level, Emotional intelligence is enhanced with age and experience. Students of M.Phil. and MA/MSc. are emotionally well aware and stronger than the students of BA/BSc.

Keywords: Emotional Intelligence EI, LEAS, HEC ranking, Emotional awareness

PMECP-23

MY SPADE: Malaysian tool for *Streptococcus pneumoniae* archives, diagnostics, and evaluation

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Streptococcus pneumoniae (*S. pneumoniae*) is the prominent bacteria causing bacteremia, community-acquired pneumonia, meningitis, and otitis media, worldwide. The burden of invasive pneumococcal disease (IPD) mainly implicates toddlers (<2 years), elderly adults (>65 years), and those with underlying comorbidities. The world health organization (WHO) ranked *S. pneumoniae* at 12th among censorious bacteria and placed pneumonia at 6th among the major cause of morbidity and mortality. In the age of modern technology, where a software application platform becomes a necessity for knowledge sharing, assessment, and awareness, no software widget standout specifically for *S. pneumoniae*. An application is developed for awareness against *S. pneumoniae* epidemiology, invasion route, symptoms, diagnosis, virulence factors, serotypes, and available vaccines to fill out the vital space. A questionnaire-based assessment method, well-trained with neural networking, is embedded for preliminary screening of pneumonia severity based on the medical health conditions of a person. Six critical questions containing medical terms of pneumonia are used in the assessment, which help professionals determine patients' condition and suggest medicine combinations with doses based on several cases. Moreover, dynamic web links are integrated into one place to provide literature and news of novel research, medicines, serotype switching, and antibiotic resistance of *S. pneumoniae*. To the best of our knowledge, this is the first application developed in Malaysian and English language, at the same time to curate, collect and analyse data from Malaysia and Pakistan.

Keywords: Streptococcus Pneumoniae, MY SPADE, Streptococcus Pneumoniae Assessment tool, Questionaire-based method

PMECP-25

A qualitative study of health professions and medical students' perspective on "Success and its attainment": A study from Mauritius

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Success is a universally understood notion, with countless perceptions. Its universality allows it to be used as a baseline to better understand and facilitate the interactions between individuals more specifically the interactions between educators and students. To do so, the true meaning of success must be elucidated. The objective of this study was therefore to delineate what undergraduate medical students and teaching faculty perceive success to be. A descriptive phenomenological qualitative study was designed and conducted on educators and medical students in Sir Seewoosagur Ramgoolam Medical College, Mauritius from August to September 2020. A total number of twenty interviews were conducted, (n=20) which consisted of 10(50%) teaching faculty and 10(50%) undergraduate medical students. NVivo 12 Plus [windows] software was utilized for the data analysis. The nodes generated were motivations, accomplishment, satisfaction, extrinsic factors, intrinsic factors and actions which were identified in the transcribed data. Satisfaction was reported as positive emotions and notions intimately related with success. Accomplishment as the fruition of any emotional, physical, mental, social, occupational and personal goals. Actions being the physical processes, acts of planning, setting of goals or forethinking exercised. Motivations being the drive to accomplish the pre-established goal. Extrinsic Factors were the external determinants and definition of success perceived by individuals. Intrinsic Factors were the subject's innate organic, understanding and definition of success. The themes generated were concepts of success, products of success and mechanisms of success. A delineation is present between the preconceived general impression of success and the wide multifactorial

cohort of extrinsic and intrinsic factors coupled to the highly emotional aspects which were brought forth by both faculty and students.

Keywords: Academic Success, Islands, Natural Science Disciplines, Psychology, Psychiatry and Psychology Category

PMECP-26

Medical student's perspectives on absenteeism: A cross sectional study from a private medical college in Mauritius

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Absenteeism has led not only to students having less understanding of the knowledge in their course, but also to students being disbarred from attempting their examinations if they have not met the necessary prescribed attendance criteria. The objective of this study was to identify the perceptions of medical students on reasons as to why absenteeism occurs and the factors to improve absenteeism. A cross-sectional observational study was conducted among 700 students from August-September 2018 at Seewoosagur Ramgoolam Medical College, Mauritius. 503 students participated in the study, which gives an overall response of 71.85%. Factors for absenteeism were weather 67%, lack of motivation 53.3%, self-studying 57.5%, health problems 56.1% and lecture timetables 61.3%, homesickness (South African students) 53.4%. However, factors that reduced absenteeism were student counselling 65.8%, active lecture engagement 91.5%, clear and logical lectures 96.8%, (especially in the department of Pharmacology, where particularly technical information is difficult for students to learn for the first time, then remember long term) reduced teaching hours 83.9%, peer mentoring by classmates and senior students 59.2% and seminars conducted by students with high absentee rates of 64.21%. It was found that the female cohort quantified peer mentoring by classmates and senior students aOR 1.506 [1.046-2.170], monthly counselling by the department aOR 1.122 [0.771-1.631], seminars conducted by students with high absentee rate aOR1. 262 [0.870-1.831] will improve their attendance as compared to male students. This study is of extreme importance as it recognizes and highlights that factors that precipitate absenteeism should be

eliminated or rectified, and that factors that decrease absenteeism should be readily employed, as lecture attendance is the foremost step in the creation of astute knowledgeable doctors.

Keywords: Anthropology, Education, Indian ocean islands, Persons Category, Psychiatry and Psychology Category, Sociology and Social Phenomena Category

PMECP-27

Effectiveness of real-time feedback system during Cardiopulmonary pulmonary resuscitation (CPR) training on performing quality CPR

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Quality cardiopulmonary resuscitation (CPR) is pivotal to ensure survival from cardiac arrest. Since the past decade, survival rate from out-of-hospital cardiac arrest is low (22.5%). The situation worsens with arising anxiety to perform CPR at out-of-hospital settings during Covid-19 pandemic. CPR trainings for layman to ensure quality chest compressions is now a global priority. This study assessed the effectiveness of CPR training with real-time feedback system compared to a standard instructor-based feedback for chest compressions acquisition among layman. Sampling frame include 120 volunteers from around Klang Valley who were certified healthy by a medical specialist, have no background of health-related field, received secondary education of at least Malaysian Certificate of Education (MCE) and literate to receive instructions in English and Malay languages. Subjects received two sessions of trainings and evaluation; the first session comprised of a standard instructor-based feedback and the second session include a real-time feedback system during chest compressions with the guide of an instructor. After training sessions, subjects performed a 2-minute chest compressions CPR and must reach a minimum technical skill level before assessments were conducted. Results showed that the quality of CPR following the standard training was moderate with the mean of compression depth, compression rate and percentage for complete chest recoil were 4.0+1.0 cm, 123.3+26.8 compressions per minute and 4.7+14.4%, respectively. The results improved when subjects performed chest compression assisted with real-time CPR feedback system; mean of compression depth is 5.5+0.4 cm, compression rate is 113.5+7.8 per minute and percentage for complete chest recoil rose to 58.9+26.1%. Paired *t*-test revealed significant differences between CPR performed with and without the feedback system for all parameters ($p<0.001$). In conclusion, incorporation

of real-time feedback system during training enhanced the quality of CPR among layman with no health-related background.

Keywords: Cardiopulmonary resuscitation, CPR, Pandemic, Cardiac Arrest, OHCA

OMD-01

Effect of palm oil-derived tocotrienol-rich fraction on angiogenesis-related gene expression in streptozotocin-induced diabetic retinopathy in rats

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Diabetic retinopathy (DR) is the common microvascular complication of hyperglycemia and remains one of the leading causes of blindness in adults around the world. Retinal angiogenesis plays a significant role in the pathophysiology of DR. Vascular endothelial growth factor (VEGF) and insulin-like growth factor 1 (IGF-1) are known to be involved in diabetic retinal angiogenesis. Compounds with anti-angiogenic properties have the potential to be used as treatment for DR. Therefore, in this study, we evaluated the effect of tocotrienol-rich fraction (TRF), an antioxidant with anti-angiogenic properties, against increased retinal VEGF and IGF-1 gene expression in rats with streptozotocin (STZ)-induced DR. Male *Sprague Dawley* rats weighing 200-250 g were divided into three groups; control group (N) received intraperitoneal (IP) injection of citrate buffer, whereas, diabetic-vehicle (DV) and diabetic-treated (DT) groups received IP injection of STZ (55 mg/kg body weight) to induce diabetes. DT received TRF (100 mg/kg body weight), whereas N and DV received olive oil as vehicle. Treatment was once daily via oral gavage for 12 weeks. At the end of the experimental period, rats were sacrificed, and retinas were collected for VEGF and IGF-1 gene expression measurement using reverse transcription quantitative real-time polymerase chain reaction (RT-qPCR). Retinal VEGF and IGF-1 expression levels in DV were higher compared to N ($p<0.001$). Retinal VEGF expression in DT was significantly lower compared to DV ($p<0.01$), however, the retinal IGF-1 expression in this group did not

differ from DV. In conclusion, oral administration of TRF reduces retinal VEGF gene expression in rats with STZ-induced DR.

Keywords: Oral, VEGF, IGF-1, Tocotrienol-rich fraction, Diabetic retinopathy, Angiogenesis, Gene

OMD-02

Salivary proteins proteomic identification is associated with subsequent allergic diseases in childhood

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Allergic disease has risen to epidemic proportions during recent years. Evidence shows that prenatal events play a critical role in determining disease susceptibility via environmental influences on placental function and fetal programming. We hypothesize that childhood susceptibility to allergy is increased through significant alterations in placental gene expression and products of identified genes altered in the saliva of allergic children. We already identified the proteins associated with childhood allergy using placental tissue whose children have different risks of allergic disease susceptibility. Then, we will determine whether these altered genes are detectable in the children's salivary proteins. The objectives of the study were to identify salivary proteins that could be a potential biomarker to identify allergy risk in newborns, and to identify target proteins for early allergy interventions. The saliva was examined using a proteomic approach that involves quantitative label-free comparative MS and data analysis is performed using Mascot database and MaxQuant software. Salivas from children without allergy were compared to children with allergic diseases (n=18). Six candidate proteins were identified in saliva samples associated with subsequent allergic disease in childhood. Five proteins identified were present in all the allergic phenotypes that include Human Mucin-5B and Human Mucin 5AC with the ratio of >2 and Human Serum Albumin, Human Serotransferrin and Human Triosephosphate Isomerase with the ratio <0.5-fold change relative to non-allergic samples.

The current findings suggest protein expression can be altered *in-utero* in children who subsequently develop an allergy and the altered expressions of these proteins are detectable in saliva in early life.

Keywords: Allergic diseases, Prenatal events, Placental functions, Fetal programming, Salivary proteins, Protein biomarker, Proteomics

OMD-05

Insulin-loaded inorganic particles in managing hyperglycaemia orally in diabetic rats

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Oral delivery is considered as most preferred and yet most challenging mode of drug administration. Fragile and sensitive peptide, like insulin shows extremely low bioavailability through Gastro-Intestinal route (GIT). To address this problem, we have designed a novel drug delivery system (DDS) using inorganic salt particle that can load and transport insulin through GIT. Empty Barium (Ba) salt particles and insulin-loaded particles were morphologically assessed and characterized using FE-SEM and FT-IR. Finally, the effectiveness of nano-insulin was tested on streptozotocin-induced diabetic rats. Ba salt particles ($BaSO_4$ and $BaCO_3$) showed very good loading of insulin (>70%) and a good degree of resistance against pH change. FT-IR peaks and FE-SEM micrograph confirmed particle formation and insulin loading. A short acting human insulin analogue, insulin aspart was loaded into Ba salt particles at a dose of 100IU/Kg for oral administration. Insulin aspart-loaded BaSO4 and $BaCO_3$ particles dramatically reduced the existing hyperglycaemia in all of rats. BaSO4 with loaded insulin showed an onset of glucose-lowering action within 1 hr, with blood glucose level measured significantly lower compared to the 2nd and 3rd hr ($p<0.05$). Insulin-loaded $BaCO_3$ particles showed a significant decrease of blood glucose level at 1-2 hrs, although the glucose level started to show slight rise at 3rd hr. By the 4th hr, it declined to the base-line level. Therefore, oral formulations of insulin/$BaSO_4$ and insulin/$BaCO_3$ particles were observed as effective as native insulin aspart subcutaneous formulation in terms of onset and duration of action. Further investigation will be needed to reveal bioavailability and mechanism of action of this novel nano-insulin formulations.

Keywords: Oral Insulin, Nanoparticle, Drug delivery system, Hyperglycemia, Ba-salt particle

OMD-06

Effects of Profortil® on leptin-induced adverse effects on the male reproductive system in Sprague-Dawley rats

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The aim of this study was to examine if Profortil®, an antioxidant micronutrient supplement, was able to prevent leptin-induced adverse effects on the male reproductive system of rats. Sprague-Dawley rats were divided into four groups: group one (Control) was treated with normal saline (0.1ml), group two (LEP) was treated with leptin (60µg/kg/day), group three (PRF) was treated with Profortil® (50mg/kg/day), and group four (LEP+PRF) was treated with both leptin (60µg/kg/day) and Profortil® (50mg/kg/day). Treatment was given once daily via the intraperitoneal route. Leptin was given for two weeks and Profortil® for three weeks. Total sperm count, abnormal sperm morphology, testicular concentration of testosterone, CYP17a1, CYP19a1, 17-βHSD, total antioxidant capacity (TAC) and 8-OHdG, and activities of SOD and catalase were measured in the testis. TUNEL assay was also performed to examine cellular apoptosis. Profortil® increased the total sperm count but showed no significant effect on the fraction of sperm with abnormal morphology. Profortil® also prevented leptin-induced increase in 8-OHdG levels. Profortil® had no significant effects on the concentration of testosterone and the enzymes involved in its biosynthesis in all groups. Similarly, no significant difference was observed in TAC or SOD activity between the four groups. Catalase activity was significantly lower, while the apoptotic index was significantly higher in LEP+PRF than that in PRF group. Treatment with Profortil® was able to reduce some of the adverse effects of leptin on some of the parameters in the testis and spermatozoa.

Keywords: Leptin, Profortil®, Sperm, Oxidative stress, Male infertility

OMD-07

Development and optimization of nanostructured lipid carriers loaded with quercetin

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Quercetin (QC) is a flavonoid that has antitumor, antiangiogenic and antibacterial activity that effectively reduces the development of biofilms by inhibiting the expression of associated genes. Despite this drug has a dissolution rate-limited oral bioavailability. In the present study, an attempt has been made to prepare nanostructured lipid carriers (NLCs) of QC to improve its oral bioavailability. The NLCs were fabricated by using high-pressure homogenization technique followed by probe sonication in which glyceryl monostearate (GMS) was used as solid lipid, Capmul MCM as liquid lipid, Tween-80 as surfactant and Transcutol-P as co-surfactant in the ratio of 1:1. The prepared NLCs were optimized by using a central composite design (CCD). The optimization results revealed that QC-NLCs exhibited a particle size of 93.01 nm, zeta potential of -15.8 mV and entrapment efficiency of 94.2%. The *in vitro* drug release study showed that only 19% of QC got released from its raw form in 12 hours. The NLCs showed a sustained release profile for QC. About 98.96% drug release of QC was observed in 12 hours from NLCs. Hence, it was concluded that the drug release of QC can be enhanced by formulating NLCs which is further indicative of enhanced bioavailability of BCS class II drugs such as QC.

Keywords: Nanostructured lipid carriers, Central composite design, *In vitro* release

PMD-02

The relationship between non-alcoholic fatty liver disease and alzheimer's disease: A computational molecular network study

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The prevalence of non-alcoholic fatty liver disease (NAFLD) increases dramatically worldwide and represents a serious medical problem. Several recent human and animal studies connected NAFLD with Alzheimer's disease (AD). Alzheimer's disease is characterized by neuropathogenesis, including synaptic and neuronal degeneration, neurofibrillary tangles and amyloid plaques, primarily composed of amyloid-beta peptide accumulates in the AD patients' brains. However, the mechanism of the relation between the two diseases is still not fully understood. Some studies connected that to the impairment of blood-brain-barrier (BBB) function among NAFLD patients or extrahepatic neurological complications resulting from NAFLD's complex interfered pathogenesis component (e.g., insulin resistance, and inflammatory reactions). This study aims to use the emerging computational bioinformatics tool to explore the molecular relationships between NAFLD and AD. The genes related to AD and NAFLD were identified by KEGG and OMIM platforms. Furthermore, genes enrichment analysis was performed using the REACTOME database to cluster the genes based on the cellular pathways (FDR <0.05). Totally 130 genes were associated with AD, and 359 were NAFLD-related genes. Enrichment analysis showed that the two diseases shared 11 pathways, including SUMOylation of intracellular receptors, activation of N-methyl-D-aspartate (NMDA) receptors and postsynaptic events, macroautophagic, autophagy, neurotransmitter receptors and postsynaptic signal transmission, transmission across chemical synapses, diseases of signal transduction, signalling by receptor tyrosine kinase, haemostasis, signal transduction, and immune system. NAFLD and AD appear to be linked indirectly by sharing the general cellular process,

such as inflammation and haemostasis. On the other hand, both diseases comprise direct neurological-related pathways, such as activation of NMDA receptors involved in synaptic plasticity pertaining to learning and memory. Besides, altering neurotransmitter receptors transmission indicates a strong direct relationship between metabolic disorders and neurological diseases, which warrants further experimental investigations.

Keywords: NAFLD, Alzheimer's Disease, Neurological Disorders, Systems Pharmacology, Pathway Analysis, Gene enrichment analysis

PMD-03

Age and gender association of BMI in obese subjects in Pakistan

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Obesity is a rapidly increasing public health problem globally associated with chronic diseases like type-II diabetes and cardiovascular diseases. The aim of this study was to assess the obesity prevalence in Lahore, Punjab, Pakistan. This cross-sectional study was carried out in Jan 2021. Data was collected through an electronic questionnaire. A total of 868 individuals (84.3% females and 15.7% males) participated. Anthropometrics; weight, height, and age were taken in kilogram (kg) centimeter (cm) and years, respectively. The standard equation to calculate BMI was used (weight in kg/height in m^2). WHO BMI cut points for Asians were used to assess the nutritional status. Statistical analysis was carried out through Microsoft Excel and SPSS (Statistical Package for the Social Sciences). Prevalence of obesity was 17.2% (12% type I obesity, 2.6 type II and type III obesity), 15.1% participants were overweight, 22.7% underweight, and 44.9% were normal. Prevalence of underweight, overweight, type I, II, and type III obesity were more in females (20.6%, 12.3%, 9.2%, 2.3%, 2%) than males (2.1%, 2.8%, 2.8%, 0.3%, 0.7%) and a positive association was found (p-value <0.05). The highest prevalence of underweight, overweight, type I, type II, and Type III obesity was observed between age group 19-21 years (11.1%, 7.3%, 7.4%, 1.5%, and 2.1%), and a positive association was observed (p-value <0.05). These results will help develop public health programs and preventive measures to reduce the prevalence of these risk factors against chronic diseases like type-II diabetes and cardiovascular diseases.

Keywords: Obesity in Pakistan, Gender and obesity, Age and obesity, Prevalence of obesity in Pakistan

PMD-05

Ethanol dysregulates bone remodelling protein expression and impairs femur cortical bone quality in alcohol rat model

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Alcohol is detrimental to bone. However, some studies have shown that moderate alcohol intake enhances bone health. Due to data discrepancy, this study investigates the effects of ethanol on bone morphology, strength and bone remodelling protein expression in alcohol rat model. 30 male Wistar rats were randomized into baseline (Bs); normal control (NC), acute alcohol (AA), chronic alcohol (CA) and alcohol withdrawal (AW). NC and AA received intraperitoneal saline and 2.5% ethanol on day 28 respectively. Whereas, CA and AW were treated with modified liquid diet (MLD) mixed with gradual alcohol concentration from day 8 until day 27 and received 2.5% intraperitoneal ethanol on day 28 before being sacrificed after 1 and 6 hours respectively. AA demonstrated a significant low total cross sectional area (Tt.Ar) and cortical area (Ct.Ar) of left femur in comparison to Bs and CA. Cortical area fraction (Ct.Ar/Tt.Ar) in AA was significantly low compared to NC, CA and AW. CA showed the lowest osteocalcin (OC) protein expression while RANKL expression was highest in AA. Acute and chronic alcohol consumption has deleterious effect on bone health evidenced by reduced bone cortical quality and disruption in bone remodelling protein expression.

Keywords: Bone microstructure, Bone strength, Osteoporosis, Osteocalcin, RANKL

PMD-06

Effects of tocotrienol-rich fraction vitamin E on non-alcoholic fatty liver disease in obese children and adolescents

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The prevalence of non-alcoholic fatty liver disease (NAFLD) is growing rapidly among children, alongside the high prevalence of obesity. Currently, there is no pharmacological agent that is available to treat NAFLD. Oxidative stress is the underlying hepatocellular injury in NAFLD. The aim of this study was to determine the effects of tocotrienol-rich fraction vitamin E (Tri-E) supplementation in childhood obesity with NAFLD. This is a single-blinded clinical trial consisted of children aged between 10 to 17 years old diagnosed with NAFLD. They were randomized into vitamin E or placebo group. Vitamin E group was supplemented with 50 mg of Tri-E daily for 24 weeks, while the placebo group received a similar tablet without Tri-E. Liver activity, and steatosis was assessed using 10 biomarkers and algorithm technology to determine the fibrosis state, combined with FibroScan at the baseline and 6-month post-intervention. DNA damage was examined using a comet assay. Twenty-nine patients were recruited, n=15 vitamin E and n=14 in the placebo group for six months duration. There was significantly lower in serum apolipoprotein A1 and aspartate aminotransferase (AST) level after six months Tri-E supplementation from 1.4 $\pm$ 0.1 (baseline) to 1.0 $\pm$ 0.3 (post) and 31.60 $\pm$ 15.0 (baseline) to 27.4 $\pm$ 12.9 (post); $p < 0.05$ respectively. There was no significant difference observed in other serum biomarkers. Fibroscan results of vitamin E group patients showed a reduction in the CAP score at six months compared to the baseline, but it was not statistically significant. Comet assay analysis showed there was a significant reduction in the DNA damage in the vitamin E group in the post-supplementation as compared to the baseline; $p < 0.05$).

In conclusion, oral Tri-E is safe for obese children with NAFLD. It has a potential lipid lowering, hepatoprotective and anti-oxidant effects.

Keywords: Non-alcoholic fatty liver disease, Vitamin E tocotrienol, Obesity children

PMD-07

Anticancer potential of Aloe-emodin and its derivatives *in-vitro* and *in-silico* perspectives

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Aloe-emodin (AE) is a hydroxyanthraquinone compound that is extracted from *Aloe vera* leaves, *Socotrine aloe*, *Rhamnus franglus* among other plants. AE has many biological activities such as antioxidant, antibacterial, anti-inflammatory and anti-cancer properties. This study aimed to review the anti-cancer activities of AE and its derivatives *in-vitro* and *in-silico* in order to examine the potential efficacy against different pathways of new derivatives conducted with molecular docking studies. All relevant studies were searched using the following databases: Web of Science, Pubmed, Scopus, Embase, as well as pre-print servers such as MDPI Preprints and ChemRxiv. The search terms aloe-emodin, aloe-emodin derivatives and cancer were combined using Boolean operators. AE or Rhubarberone was found to have anti-tumor properties against gastric, neuroectodermal, breast, liver and colon cancer cell lines by cell cycle arrest at G0/G1 phase and apoptosis induction. Specifically, the greater number of oxygen atoms and hydroxyl groups increase cell permeability for these compounds and thus, their efficacy. Furthermore, acidic substitution with phenolic or carboxylic groups at the position C-6 may also contribute to the anti-angiogenic potency. In addition, Pyrole-linked AE induced early and late apoptosis in breast cancer cell lines. In-silico-designed trihydroxy benzene group on C-1 of the AE structure expected a superior activity and high affinity on Bax protein that is known as pro-apoptic protein in many cancer cases. In conclusion, AE derivatives were reported to exert higher anticancer effect than the original compound, and the triazole

derivatives of AE demonstrated great further potential for further *in-silico* and *in-vitro* investigation.

Keywords: Aloe-emodin, Derivatives, *In-silico, In-vitro*, Cancer, Apoptosis

PMD-08

Chalcones and their derivatives: A bibliometric analysis

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Chalcones is a group of aromatic chemical compounds that has anti-bacterial, anti-fungal, anti-tumour, anti-inflammatory, and anti-cancer activities as their main characteristics in this study. This study aimed to analyse the main characteristics of chalcones and its derivatives and identify the top-cited articles published on suggested topic. All relevant studies with regard to chalcones until January 2021 were extracted from Web of Science, Scopus, and PubMed. VOSviewer and Endnote were used to collect and analyse the publications on their main characteristics and identify articles with the highest citation rate. There were 37678 publications from inception of database until March 2021. Most of the articles (38.31%) were focused on chemistry, followed by biochemistry (21.32%) and pharmacology (13.51%). The most common keywords were humans; chalcones; animals; acyltransferases; flavonoids; chalcone; gene expression regulation, plant; plant proteins; cell line, tumor; molecular structure. Most studies on chalcones were conducted on the subject of chemistry and plants, with little research done on the pharmacological properties. Due to its use in Asia products, more studies were conducted in Asia than other continents.

Keywords: Bibliometrics, Citation, Chalcones, Plant-derived polyphenolic, Flavonoids

PMD-11

A study on knowledge, attitude and practice (KAP) regarding diabetes mellitus among rohingya refugees attending imaret mobile clinic

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About 88,880 Rohingyas have been registered with UNHCR in Malaysia and increasingly in number. Diabetes mellitus (DM) is a chronic disease associated with abnormally high levels of the sugar glucose in the blood. It is the most concern disease globally and have showed an increase in prevalence pattern of diabetes mellitus with longer migration history for the Rohingya refugee. If uncontrolled, diabetes mellitus can be the cause of damage to the eyes and potentially cause blindness, damage to the kidneys which may lead to renal failure, and damage to nerves. Diabetes mellitus believe to be a silent disease, this is when the diabetic patient recognize that they have diabetes mellitus after one of its life-threatening complications had developed. To determine the knowledge, attitude and practice (KAP) regarding Diabetes mellitus among Rohingya refugees attending IMARET mobile clinic. This study was a cross sectional study. Structure questionnaires were used and respondents were interviewed with the help of translator. Data were analyzed using SPSS version 25.0. Independent t-test, ANOVA test and correlations test were used. A total of 56 respondents participated in this study. Majority of respondents was female (73.2%), majority in age group between 31-40 years, married (83.9%), and 21.4% have diabetes mellitus. There were significant differences of knowledge between respondents with history of diabetes mellitus ($p<0.001$). Meanwhile there were significant mean differences of attitude score between history of DM ($p<0.001$) and marital status ($p=0.008$) respondents with history of diabetes mellitus. There were significant mean differences of practice

score between history of DM (p=0.039) and between different occupation (p=0.037). There was a moderate score of knowledge, good positive attitude, and moderate score of practice towards diabetes mellitus.

Keywords: Rohingya refugee, Refugee, Diabetes mellitus, Knowledge, Attitude, Practice, IMARET mobile clinic

ONPIM-01

Phytochemical composition and antioxidant properties on bark of *Litsea garciae*

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The plants of the Litsea genus are widely explored concerning their nutritional and medicinal purposes. The recent study investigated the antioxidant capabilities and phytochemical composition of *Litsea garciae* (LG) bark's hexane, chloroform, methanol, and aqueous extracts. Antioxidant measurements were performed by determining the total phenolic content (TPC) and the total flavonoid content (TFC). Antioxidant capacities were assessed employing free radical scavenging (DPPH assay) and ferric reducing power (FRAP assay). The secondary metabolites composition was evaluated by Ultra-High-Performance Liquid Chromatography-Mass Spectrometry (UHPLC-MS) method. As a result, methanol extract was recorded to have the highest TPC value aligned with its positive appearance in phytochemical screening. Its antioxidant capacity indicated the least IC50. Results showed that the significant free radical scavenging activity was related to the presence of high phenolic content in the methanolic extract. UHPLC-MS analysis revealed significant variation in the secondary metabolites present in the methanol extract. The major phenolic compounds were found including N-trans-feruloyl-4-O-methyldopamine, N-cis-feruloyltyramine, epicatechin-(4beta->6)-epicatechin-(2beta->7,4beta->8)-epicatechin, 7-Hydroxy-3-(4-methoxyphenyl)-4-propyl-2H-1-benzopyran-2-one and 9-O-Methylneodunol. Overall, results have suggested LG bark to be a lead source for novel natural products possessing antioxidative potential.

Keywords: Hexane, Chloroform, Methanol, Aqueous, *Litsea garciae* (LG) bark, Antioxidant, Phenolic compounds

ONPIM-02

Proteomics, toxicity and cross-neutralization of the venom of samar cobra (*Naja Samarensis*) from the Southern Philippines

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Samar cobra, *Naja samarensis* (NS), is a medically important venomous snake in the Southern Philippines. Envenomation by NS produces paralysis leading to asphyxial death, yet there is no species-specific antivenom. Furthermore, the composition and toxicity of NS venom have not been investigated, limiting our understanding of the pathophysiology of envenomation. This study aimed to investigate the venom proteome of NS venom, and to examine the efficacy of a hetero-specific antivenom raised against *Naja philippinensis* in cross-neutralizing the NS venom and principal toxins. NS venom proteome was studied using C18 reversed-phase high-performance liquid chromatography, sodium dodecyl sulfate-polyacrylamide gel electrophoresis and liquid chromatography-tandem mass spectrometry. Immunoreactivity of the Philippine Cobra Antivenom (PCAV) toward venom and fractions was examined with enzyme-linked immunosorbent assay (ELISA). Toxicity and neutralization of NS venom and principal toxins by PCAV was assessed in a mouse model. Proteomics resulted in a domination of three-finger toxins (3FTx, 90.48%), predominantly short alpha-neurotoxins (SαNTX, 65.87%) and cytotoxins (CTX, 16.29%). In ELISA, PCAV showed modest immunogenicity towards NS venom and principal toxins, implying conserved antigenicity between the Philippine cobras. The NS venom was highly lethal (LD50 = 0.20 µg/g), predominantly driven by SαNTX (LD50 = 0.18 µg/g). PCAV cross-neutralized the lethality of NS venom and SαNTX, albeit with low potencies,

0.17 mg venom and 0.20 mg SαNTX/ml antivenom. PCAV was immunoreactive and able to cross-neutralize the lethality of NS venom and SαNTX with limited efficacy. PCAV is clinically useful for NS envenomation, yet improvement of species coverage and potency of neutralization is needed.

Keywords: *Naja samarensis*, Snake venom, Venomics, Antivenom

ONPIM-03

Cytotoxic effects, antioxidant capacity & collagenase content of *bedak sejuk* (cooling powder) made from *Oryza sativa ssp. indica* & *Oryza sativa ssp. japonica* on UVB-induced B164A5 melanoma

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Bedak sejuk is a traditionally fermented rice-based cosmetic product that is applied topically as an overnight facial mask to gain skin health benefits. Hence, our study aimed to determine the effects of *bedak sejuk* made from *Oryza sativa ssp. indica* (*Indica*) and *Oryza sativa ssp. japonica* (*Japonica*) on UVB-induced B164A5 melanoma, for their cell viability, antioxidant capacities and collagenase (MMP-1) content. Firstly, via the 3-[4,5-dimethylthiazole-2-yl]-2,5-diphenyltetrazolium bromide (MTT) cell viability assay, *Indica* and *Japonica bedak sejuk* had no cytotoxic effects towards the cells. Hence, no half maximal inhibitory concentration (IC_{50}) was obtained, and the optimum doses (50 and 100 g/L) were chosen for treatment. Next, in the Ferric Reducing Antioxidant Power (FRAP) assay, 50 and 100 g/L of *Indica bedak sejuk* showed FRAP values of 0.003 $\pm$ 0.001 µg AA (ascorbic acid)/g of *bedak sejuk* and 0.004 $\pm$ 0.0003 µg AA/g of *bedak sejuk*. Whereas 50 g/L of *Japonica bedak sejuk* had the same value as 100 g/L of *Indica bedak sejuk*. As for 100 g/L of *Japonica bedak sejuk*, it showed the highest antioxidant capacity with a value of 0.01 $\pm$ 0.0007 µg AA/g of *bedak sejuk* which was statistically significant ($p < 0.05$) when compared to other tested concentrations. From the results, 100 g/L of *Indica* and *Japonica bedak sejuk* were chosen for the

mouse MMP-1 ELISA kit, and there was no significant difference for both treatments when compared to the negative control. In conclusion, with further investigations, *Indica & Japonica bedak sejuk* have potential as melanoma chemopreventive agents.

Keywords: *Bedak sejuk*, Fermented rice, Fermented cosmetics, *Oryza sativa Indica, Oryza sativa Japonica*, B164A5, Melanoma

ONPIM-04

Lignosus rhinocerotis Cooke Ryvardan reduces allergen-induced airway inflammation, hyperresponsiveness and remodelling in a mouse model of allergic asthma

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Lignosus rhinocerotis (Cooke) Ryvardan (*L. rhinocerotis*) is a medicinal mushroom which commonly used in the treatment of asthma and several other illnesses by the traditional and complementary medicine practitioners in Malaysia. In this study, the effects of *L. rhinocerotis* on allergic airway inflammation, hyperresponsiveness and remodelling were investigated. *L. rhinocerotis* extract (LRE) was prepared by hot water extraction using soxhlet. Airway hyperresponsiveness (AHR) study was performed in house dust mite (HDM)-induced asthma model; while airway inflammation and remodelling study was performed in prolonged ovalbumin (OVA)-induced airway inflammation in female Balb/C mice model. Following allergen challenge, the mice were treated with three doses of LRE (125, 250, 500 mg/kg) by oral gavage for 2, 6 and 10 weeks. Treatment with different doses of LRE significantly inhibited AHR in HDM-induced mice. Treatment with LRE also significantly decreased the elevated IgE level in serum, Th2 cytokines level in bronchoalveolar lavage fluid and ameliorated OVA-induced histological changes in mice by attenuating leukocyte infiltration, mucus hypersecretion and goblet cell hyperplasia in the lung tissues. LRE also ameliorated airway remodelling by reducing smooth muscle thickness and reducing the expressions of TGF-β1 and Activin A positive cells in the lung tissues. In conclusion, LRE attenuated airway inflammation, hyperresponsiveness and remodelling in the allergic asthma model. These findings suggest the therapeutic potential of LRE as an alternative for the management of allergic asthma.

Keywords: Allergic asthma, Hyperresponsiveness, inflammation, *Lignosus rhinocerotis*, Remodelling

ONPIM-05

Effect of tocotrienol rich fraction on retinal cell apoptosis in rats with streptozotocin-induced diabetic retinopathy

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Hyperglycaemia-induced oxidative stress is a crucial factor involved in retinal cell apoptosis associated with diabetic retinopathy. In this study, we investigated the effect of tocotrienol-rich fraction (TRF), a potent antioxidant, on retinal cell apoptosis in Sprague-Dawley rats. The rats were divided into three groups, normal rats treated with vehicle (N), diabetic group treated with vehicle (DV), diabetic group treated with TRF (DT). Diabetes was induced by intraperitoneal injection of streptozotocin. Rats that attained blood glucose levels of more than 20 mmol/L, 48 hours post-induction, were considered diabetic and included in the study. Diabetic rats were thereafter orally treated with either TRF or the vehicle. An additional group of normal rats also received oral treatment with vehicle. After 12 weeks of treatment, the rats were euthanised using intraperitoneal sodium pentobarbital and retinas were isolated to estimate the expression of pro- (caspase-3, Bax) and anti-apoptotic (Bcl-2) markers using ELISA. Significant upregulation of pro-apoptotic proteins and downregulation of anti-apoptotic proteins was observed in the diabetic vehicle treated group ($p<0.05$) compared to the vehicle treated normal rats, and TRF treated diabetic group. The expression of the same parameters in the TRF treated group was comparable to that in vehicle treated normal rats. Additionally, the Bax/Bcl-2 ratio was 1.43, 5.47 and 0.79 for normal, diabetic control and TRF treatment groups, respectively. In conclusion, oral TRF treatment protects against retinal cell apoptosis in rats with streptozotocin-induced diabetic retinopathy despite persistent hyperglycemia.

Keywords: Tocotrienol-rich fraction, Retinal cell apoptosis, Streptozotocin, Diabetic retinopathy

ONPIM-06

Flavonoids and mechanism of immunomodulation: Apigenin, luteolin and quercetin modulate natural killer cells cytokine secretion

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Natural killer (NK) cells play a crucial role to fight against viral infection and cancer through various mechanisms; among them are cytotoxic granules secretion and cytokines production. Our previous study documented that the cytotoxic effect of NK cells against lung cancer was significantly elevated after being treated with apigenin, luteolin and quercetin. In addition, the cytotoxic granules perforin and granulysin secretion was observed with apigenin and luteolin treated NK cells. Thus, this study aimed to demonstrate the cytokine production of these three flavonoids-stimulated-NK cells to find out the alternative immunomodulatory mechanism of the flavonoids on immune cells. NK cells were incubated with three flavonoid compounds at 12.5 and 25 µg/ml for apigenin and luteolin and 25 and 50 µg/ml for quercetin over 24 hours at 37°C. Both type-1 cytokines, interleukin-2 (IL- 2), interferon-gamma (IFN-γ), type-2 cytokines IL-4 and IL-10 secretion level were determined using Enzyme Link Immunosorbent Assay (ELISA). We found that the IL-2 secretion by NK cells was significantly elevated by both luteolin and quercetin treatment but not with apigenin. NK cell IFN-γ secretion was also significantly increased with luteolin 25 µg/ml concentration. In the case of NK cell IL-4 and IL-10 secretions, no significant changes were found with all three flavonoid compounds apigenin, luteolin and quercetin at all different doses. It is concluded that luteolin exerted the strongest effect on NK cells type-1 cytokines production whereas quercetin was effective to produce only IL2 release. It is concluded that some flavonoids use cytokine-mediated intracellular mechanism to fight against lung cancer cells.

Keywords: Apigenin, Luteolin, Quercetin, NK cells, Cytokines, Interleukins, Interferon-gamma

ONPIM-07

Systems pharmacology approach for interpreting the potential therapeutic mechanisms of action of *Orthosiphon aristatus*

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Orthosiphon aristatus is a popular herbal in Southeast Asia. Several studies confirmed the therapeutic benefits of its bioactive compounds, such as rosmarinic acid and sinensetin. In this study, we used computational systems pharmacology approach to predict and analyse the molecular mechanisms of action (MOA) to illustrate the targets and cellular pathways of the *O. aristatus*' bioactive compounds. *O. aristatus*' compounds were identified using the traditional Chinese medicine systems pharmacology (TCMSP) database, besides literature review, then filtered based on oral bioavailability (>50%). The corresponding human molecular targets were predicted using two different platforms (Swiss Target Prediction and BATMAN-TCM). Further, pathways enrichment analyses were performed using OMIM and KEGG databases (FDR < 0.05). Sixty-eight bioactive compounds of *O. aristatus* were filtered out of 99. A total of 876 potential targets were predicted. OMIM analysis showed involvement in many cellular processes, for example, protein kinase activity (139 genes), ATP binding (145 genes), and postsynaptic membrane (45 genes). A subsequent KEGG analysis showed a significant involvement in several diseases pathways, including cancer (90 genes), nicotine addiction (63 genes), hepatitis B (42 genes), osteoclast differentiation (35 genes), apoptosis (26 genes), and fat metabolism (9 genes). Indicating that *O. aristatus* has therapeutic benefits in many diseases through targeting multi-pathways. *O. aristatus* could mediate pharmacological effects of metabolic disorders and cancers (e.g. prostate and colorectal) through multi-target and various

signalling pathways, including kinase proteins activity and immune system-related pathways including (T & B cell receptor, TNF, and natural killer). The systems pharmacology approach predicts the molecular MOA, however, further experimental validation is required.

Keywords: *Orthosiphon aristatus*, Systems Pharmacology, Pathway Analysis, Target Prediction, Cellular Targets

ONPIM-08

Clitoria ternatea root fraction ameliorates the hippocampal synaptic plasticity in chronic cerebral hypoperfusion rat model

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Chronic cerebral hypoperfusion (CCH) is characterized by insufficient cerebral blood flow to the brain to meet its metabolic demand. This lead to hippocampal damage and eventually caused cognitive decline. *Clitoria ternatea* root extract has been shown to improve cognitive function. However, the possible mechanisms mediating its cognitive function need further investigations. In the current study, the effects of *Clitoria ternatea* root fraction and its potential mechanism were investigated on the hippocampal long-term potentiation (LTP) in CCH rat model. The *Clitoria ternatea* root fraction (CTRF) was prepared by phase column chromatography technique. The CCH rat model was established by permanent bilateral common carotid artery occlusion (2VO) in rats. The rats were divided into five groups of treatment: Sham+vehicle.; 2VO+veh.; 2VO+CTRF (10, 20 and 40mg/kg). A monopolar recording electrode was placed in CA1 (AP: -4.2 mm, ML: -3.0 mm, V: -3.0 mm) to record the field excitatory post-synaptic potential (fEPSP) and stimulating electrode was placed in the contralateral CA3 region of the hippocampus (AP: -4.2 mm, ML: +3.0 mm, V: -4.0 mm). The theta burst stimulation (5Hz) was applied to induce LTP and fEPSP was recorded for 2 hours. The brain was harvested for western blot analysis. 2VO+CTRF (40mg/kg) exhibited the most significant effect to enhance hippocampal synaptic plasticity compared to 2VO with no treatment. In addition, the decreased levels of ERK, CREB, BDNF, PSD-95 and SYNP were significantly reversed by CTRF (40mg/kg) except for CAMKIIα. Taken together, our findings suggest that CTRF alleviated

CCH-induced cognitive decline by increasing the expression of synaptic plasticity-related proteins. Hence, CTRF has the potential to be developed as a Smart Drug for the treatment of dementia-related to cerebrovascular diseases.

Keywords: Chronic cerebral hypoperfusion, *Clitoria ternatea*, Vascular dementia, Long-term potentiation, Western blot

ONPIM-10

Formulation and characterization of chitosan/β-glycerophosphate thermosensitive *in situ* gels for ocular delivery of lomefloxacin hydrochloride

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Topical eye drop is one of the most convenient and patient compliant ocular dosage forms in the treatment of anterior segment-based ocular infections. However, the drug bioavailability and therapeutic effectiveness are low due to rapid drug elimination from the pre-corneal region and nasolacrimal drainage. A frequent, multiple daily doses of lomefloxacin hydrochloride eye drops used to treat bacterial infections minimizes the patient adherence to medication and noncompliance to the treatment. This study aimed to formulate and characterize thermosensitive chitosan-β-glycerophosphate (β-GP) *in situ* gels containing lomefloxacin by cold dispersion method to overcome the limitations. *In situ* gels composed of lomefloxacin (0.3% w/v) and increased β-GP concentration from 10 to 40% at a constant chitosan concentration of 1.5% (w/v) were characterized. The gels were free-flowing, particle-free with a pH of 4.39 to 7.51. A solution to gel phase transition took place at ocular temperature (33-37°C), with gels constituting 1.5% w/v chitosan and β-GP at concentrations of 30 and 40%. The viscosity of *in situ* gels was lower at higher contents of β-GP before gelation and exhibited a higher viscosity after gelation. High β-GP content nonetheless sustained the drug release

with a low initial burst release for 8 hours via zero-order release pattern and non-fickian diffusion mechanism. Hence, the prepared sustained release *in situ* gels containing lomefloxacin conferred thermosensitive properties and may potentially improve the therapeutic efficiency including patient compliance with increased residence time at the ocular surface and reduced dosing frequency for the successful treatment of ocular infections.

Keywords: Lomefloxacin, *In situ* gels, Thermosensitive, Chitosan, β-glycerophosphate, Sustained release

ONPIM-11

Centella asiatica prevents hypertension and protects the heart in chronic nitric oxide deficiency rat model

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Hypertension is a major risk factor for cardiovascular disease (CVD) in which is the number one cause of mortality globally. *Centella asiatica* belongs to the plant family Apiaceae (Umbelliferae) and it contains a high amount of triterpenoid and flavonoid which have antioxidant properties and are involved in the renin-angiotensin-aldosterone system (RAAS), an important hormonal system for blood pressure regulation. This study aimed to investigate the effects of *C. asiatica* extract on blood pressure and heart in hypertensive rat model, induced using oral N(G)-nitro-L-arginine methyl ester (L-NAME). Male Sprague-Dawley rats were divided into five groups. The first group received deionized water only. Groups 2, 4 and 5 were given L-NAME (40 mg/kg, orally) for eight weeks. Groups 4 and 5 concurrently received *C. asiatica* extract (500 mg/kg, orally) and captopril (5 mg/kg, orally), respectively. Group 3 only received *C. asiatica* extract. Systolic blood pressure (SBP) was measured at weeks 0, 4 and 8. After eight weeks, all rats were sacrificed, and aortic and cardiac samples were harvested for laboratory evaluation. At the end of study, *C. asiatica* extract and captopril administrations prevented the elevation of SBP and reduction in serum nitric oxide (NO) level as well as an increase in cardiac and aortic malodialdehyde (MDA) content, cardiac angiotensin-converting enzyme (ACE) activity and serum brain natriuretic peptide (BNP) level, induced by L-NAME administration ($p < 0.05$). In conclusion, *C. asiatica* extract can prevent the development of hypertension and cardiac damage induced by L-NAME, and these effects were comparable to captopril.

Keywords: *Centella asiatica*, Hypertension, Cardiac failure, L-NAME, Nitric oxide

ONPIM-12

Mitochondria protective effects of nicotine on hippocampal neurons of rapid eye movement sleep deprivation induced stress in rat model

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Depression has been shown to disturb cellular organelles, while activation of nicotinic receptors alleviates this effect. This study was conducted to investigate the protective effects of the nicotine on the mitochondria hippocampal neurons among depressed rats. While, depressed rat model was induced using rapid eye movement (REM) sleep deprivation techniques. Male Sprague-Dawley rats were divided into a normal condition, REM sleep deprivation (model of depression) and control wide platform condition for 72 hours. Throughout this procedure, 1mg/kg of saline or nicotine was given subcutaneously 12 hourly. Then, the rats were sacrificed and using transcardial perfusion fixation, the brain were harvested. The changes of the hippocampal mitochondria were determined using transmission electron microscopy (TEM). TEM showed severely damaged structure of mitochondria in hippocampal neurons of the REM sleep-deprived rats. However, nicotine treatment preserves hippocampal mitochondria structure of the REM sleep-deprived rats. Acute nicotine treatment in depression protects hippocampal neurons mitochondria ultrastructure from damage.

Keywords: Mitochondria, Nicotine, Hippocampus, Stress, Rapid eye movement, Sleep deprivation

ONPIM-14

Protective effect of *Chlorophytum borivilianum* root extract against hydrogen peroxide (H_2O_2)-induced oxidative stress on the reproductive system in male mice

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The imbalance between reactive oxygen species (ROS) and antioxidant capacity (AC) in spermatozoa causes oxidative stress; it could affect the sperm motility, morphology, deoxyribonucleic acid (DNA) integrity and fertilization. This study was aimed to investigate the protective effect of aquoeus root extract of *Chlorophytum borivilianum* against H_2O_2 induced oxidative stress on the reproductive system in male mice. ICR adult male mice were administered orally with hydrogen peroxide (H_2O_2) or *C. borivilianum* (100 and 200 mg/kg/bw). After 14 days, mice were sacrificed, blood, sperm and testes were harvested. Serum testosterone, follicle stimulating hormone (FSH) and luteinizing hormone (LH) were measured by ELISA. Sperm count, motility, viability, hyperosmotic swelling (HOS) tail-coiled sperm and morphology were evaluated. Expression of oxidative stress (4-HNE) and antioxidative markers (Nrf2, Keap-1, SOD-1, HO-1, NQO-1, NOX4, and catalase), steroidegenic marker (StAR, SHBG and aromatase) and tight junction marker (occludin, E-cadherin and integrin) in testis were determined by western blotting, immunohistochemistry and immunofluorescence. In mice receiving *C. borivilianum*, sperm count, motility, viability, HOS tail-coiled sperm increased, and abnormal sperm morphology were decreased in H_2O_2 treated mice. An elevation in serum testosterone with decreased FSH and LH. *C. borivilianum* prevented the downregulation of steroidegenic markers and tight junction markers with upregulation of oxidative stress. As a consequence of the findings, we concluded that *C. borivilianum* root extract is protective against hydrogen peroxide induced oxidative stress on the reproductive system in male mice.

Keywords: Male infertility, Oxidative stress, *Chlorophytum borivilianum*, Steroidogenesis, Tight junction

ONPIM-15

Anti-proliferative and apoptosis induction of acute lymphoblastic leukaemia cells by madecassoside

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Acute lymphoblastic leukaemia (ALL) is a blood cancer characterized by the uncontrolled proliferation of immature lymphocytes. Madecassoside is a major natural triterpenoid saponin isolated from a traditional medicinal plant *Centella asiatica (L.) Urban* that possesses anti-proliferation activity. However, the effect of madecassoside in ALL cells has never been investigated. In this study, we aimed to evaluate the anti-proliferative effect of madecassoside in CCRF-CEM ALL cells. CCRF-CEM cells were treated with different concentrations of madecassoside (from 1 to 200 μM) for 24 and 48 hours before being evaluated for cell viability with MTT assay. Cell apoptosis was determined by double staining with Annexin V-FITC/propidium iodide and detected by flow cytometric analyses. The intracellular accumulation of reactive oxygen species (ROS) and mitochondrial membrane potential (MMP) was evaluated using the fluorescent probe DCFDA and TMRE, respectively. Madecassoside treatment significantly decreases cell viability in a dose-dependent manner with an IC50 value of 40 $\pm$ 0.07 μM after 48 hours of treatment. Meanwhile, madecassoside treatment also significantly induced late apoptosis (11%) and necrosis (2.8%) in CCRF-CEM cells compared to the control group by flow cytometry. Gradual increase of ROS was also observed by time (0, 1, 2, 3 and 4 hours) as detected by the fluorescence reader. The number of TMRE-labeled red-orange cells gradually declined as the concentrations of madecassoside increased, showing an increasing attenuation of MMP level in CCRF-CEM cells. Madecassoside inhibits the viability of ALL cells by facilitating cell apoptosis and cell necrosis *via* plasma membrane blebbing and cell shrinkage.

Keywords: Madecassoside, Acute lymphoblastic leukaemia, Proliferation, Cell apoptosis

ONPIM-17

Bitter gourd honey ameliorates hepatic and renal diabetic complications on type 2 diabetes rat models by anti-oxidant, anti-inflammatory, and anti-apoptotic mechanisms

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Diabetes is one of the world's major health problem The objective of this study was to determine the anti-oxidant, inflammatory and apoptosis properties of bitter gourd honey (BGH) in streptozotocin-induced diabetic rat's kidney and liver. A single dose [Nicotinamide 110 mg/kg, streptozotocin (STZ) 55 mg/kg, intraperitoneal (i.p)] was used to induce experimental diabetes. BGH was administered orally to adult male normal or diabetic rats i.e. 1 g/kg/day and 2 g/kg/day for 28 days. At the end of the treatment blood, liver, and kidney samples were collected for biochemical, histopathology and molecular analysis. Meanwhile, Liquid chromatography–mass spectrometry (LC –MS) was used to identify the major bioactive compounds in the BGH. The administration of BGH to diabetic rats results in significant reduction in ALT, AST, creatinine and urea levels ($p<0.05$). In diabetic rats treated with BGH showed lesser histopathological changes in liver and kidney. BGH treated diabetic rats showed to decreased oxidative stress, inflammatory (MYD88, IKKβ,

NFKB, p-NFKB), apoptosis markers (caspase-3) with increased antioxidant enzymes (SOD, CAT and GPx). Many bioactive compounds in BGH exhibit anti-oxidative, anti-inflammatory, and anti-apoptotic activities. Administration of BGH to streptozotocin-induced diabetic rats could help to protect the liver and kidney against oxidative stress, inflammation and apoptosis-induced damage while preserving hepatic and renal function near normal in diabetes.

Key words: Diabetes mellitus, Oxidative stress, Antioxidant enzymes, Inflammation

ONPIM-18

Rutin loaded liquid crystalline nanoparticles attenuate oxidative stress in bronchial epithelial cells

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The research aimed to formulate Rutin loaded liquid crystalline nanoparticles (LCNs) followed by its physicochemical characterisation, *in vitro* release study, and investigating its inhibitory potential on oxidative stress in human bronchial epithelial cells (BEAS-2B). The Rutin LCNs were prepared by ultra-sonication method and evaluated for particle size, polydispersity index (PDI), and zeta potential and entrapment efficiency. *In-vitro* release was studied through the dialysis bag technique. Further, the inhibitory potential of Rutin-loaded LCNs on oxidative stress was determined in BEAS-2B by analysing the expression levels of oxidative stress associated genes. Rutin was successfully encapsulated into LCNs having a mean particle size of 130 nm along with polydispersity index of less than 3, and zeta potential of -25mV. Encapsulation efficiency findings revealed that approximately 70% of Rutin was encapsulated in LCNs. Nanoparticles were observed spherical in shape, demonstrated sustained release pattern and also inhibited the genes causing oxidative stress, namely, Nox2B and Nox4 in BEAS-2B cells. In addition, the LCNs further demonstrated an upregulation of Gclc and Nqo-1 (antioxidant genes) expression in a dose-dependent manner. Our findings indicate the promising potential of Rutin-loaded LCNs as an effective treatment strategy in patients with high oxidant loads, in various respiratory diseases.

Keywords: Rutin, Antioxidant, Nanoparticles, Oxidative stress, Inflammation

ONPIM-19

In vitro angiotensin-converting enzyme (ACE) inhibition activity of *Syzygium polyanthum* leaves and its inhibition mechanism

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Syzygium polyanthum is an ethnomedicinal plant with significant antihypertensive effect; however, the mechanism of action is not yet well-described. This study aims to investigate one of its possible antihypertensive mechanisms, the angiotensin-converting enzyme (ACE) inhibition and its inhibition mechanism. *S. polyanthum* leaves were macerated using water, methanol, ethyl acetate, and hexane to produce the aqueous (ASP), methanolic (MSP), ethyl acetate (EASP) and hexane (HSP) extracts. Each extract (100 µg/ml) was screened for *in vitro* ACE inhibition activity according to Cushman and Cheung assay method. The standard drug, captopril (2.06 ng/ml) was used as a positive control. The most active extract was further tested at 1 to 1000 µg/ml to determine its potency. A similar assay was then conducted in the presence of zinc chloride or bovine serum albumin (BSA) to determine ASP's ACE inhibition mechanism. ASP was found to exhibit the highest inhibition activity (69.43 $\pm$ 0.60 %), followed by HSP (45.40 $\pm$ 0.15 %), MSP (41.63 $\pm$ 0.15 %), and EASP (9.62 $\pm$ 1.60 %). The concentration of ASP that caused 50 % ACE inhibition activity (IC50) was 41 µg/ml. ASP's ACE inhibition activity was significantly reduced with the presence of BSA but not significantly affected by the presence of zinc chloride. In conclusion, *S. polyanthum* leaves

possessed a significant ACE inhibition activity which was majorly present in its aqueous extract. It is postulated that ASP's ACE inhibition activity was due to its ability to conjugate with protein, and it was non-dependent on the zinc at the ACE active site.

Keywords: Angiotensin-converting enzyme, Antihypertensive, Hypertension, *Syzygium polyanthum*

OPNIM-20

Chrysin and lentinan chemosensitize temozolomide in GBM

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The high GBM tumor heterogeneity and complex tumor microenvironment often lead to chemo-radioresistant, leading to an abysmal prognosis. Natural products which are multitarget may enhance the current chemotherapy (Temozolomide; Tmz) efficacy. Although, chrysin and lentinan have been tested as a potential adjuvant in different cancer models, their synergistic effect against Tmz in human GBM has never been reported. Chrysin and Lentinan single treatment reduced the GBM cell viability while the combination of chrysin or lentinan to Tmz further enhanced cell death (CI indexes between 0.35 – 0.98), suggesting their synergistic efficacy. Both chrysin or lentinan promoted Tmz-induced phosphatidylserine externalization and depolarization of mitochondrial membrane potential. Interestingly, the co-treatment of lentinan with Tmz reduced the induction of necrosis in Tmz. The addition of lentinan to Tmz treatment further modulated anti- and proapoptotic proteins, Bcl-xL, with concomitant caspase activation 3 and 9. Meanwhile, chrysin addition targeted the suppression of pAkt and pERK1/2 while enhanced the p38 MAPK phosphorylation, which reduced anti- and proapoptotic proteins and activated caspase-9 and -3. However, this was reversed by the Z-LEHD-FMK, Z-VAD-FMK and SB 202190 while further promoted by API-2 and U0126. The current study demonstrated chrysin and lentinan synergistically promoted Tmz anticancer effects by promoting the intrinsic apoptosis through caspase activation. Collectively, the data may suggest chrysin and lentinan as an affordable and effective nutraceutical-based adjuvant to improve Tmz efficacy in GBM. By doing so, we are currently moving to further elucidate the mechanisms *in vitro*, 3D and animal models.

Keywords: Chrysin, Lentinan, Glioblastoma, Apoptosis, Temozolomide, Nutraceutical, Adjuvant

ONPIM-21

Elucidating the effectiveness of Red Palm Oil (RPO) in preventing oxidative stress level in Polycystic Ovarian Syndrome (PCOS) induced rats

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Red palm oil has a variety of medicinal applications due to its high nutritional value. However, till date, there is no study have been shown the effectiveness of red palm oil in alleviating oxidative stress in PCOS. In this study, the effects of Red Palm Oil on PCOS induced oxidative stress was determined. Forty *Sprague Dawley* female rats were divided into five experimental groups, each with eight rats (n=8). To induce PCOS, the rats were given 1 mg/kg of Letrozole diluted in 0.9 percent NaCl. There were no induction or treatment for the control group. Metformin dissolved in 0.9 percent NaCl (100mg/kg); was given to the positive control group, followed by letrozole. Letrozole was given to intervention Group 1 and 2 after 200mg/kg of red palm oil and 400mg/kg of red palm oil, respectively. Only Letrozole (1mg/kg diluted in 0.9 percent NaCl) was administered to negative group. After 28 days the rats were sacrificed and the oxidative stress markers (GSH, SOD, MDA and TAC) from blood serum were tested using ELISA kit. The antioxidant activities of red palm oil were determined using 2,2-diphenyl-1-picrylhydrazyl (DPPH) method. The data were analysed using SPSS (one-way ANOVA) Level of GSH, SOD and TAC in treated groups were found significantly higher compared to untreated groups ($p<0.05$). Meanwhile, level of MDA in treated group decreased as compared to untreated group ($p<0.05$). Other than that, red palm oil shown has highest antioxidant contain 1.956./100 g dry weight. Current study revealed red palm oil proven that it can help in alleviating oxidative stress level in PCOS induced rat. This is due to the antioxidant exhibited by red palm oil. Further research needs to be done to determine the association of red palm oil with other PCOS markers like hormone changes.

Keywords: Oxidative stress, PCOS, Antioxidant, Red palm oil

ONPIM-22

Anti-inflammatory mechanism of lipid mediator N-palmitoylethanolamide in ameliorating toll like receptor-4 carrageenan induced acute inflammatory pain

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Activation of TLR4 leads to increase expression of pro-inflammatory molecules that are secreted by TLR4 expressing cells to promote inflammation and sensitize primary afferent nociceptors leading to pain. Increased tissue levels of these pro-inflammatory molecules promote the infiltration of circulating neutrophils and monocytes to the site of injury that in turn caused the increasing of plasma and cell recruitment (swelling) and hyperalgesia. The fatty acid amide N-Palmitoylethanolamide (PEA) is an endogenous ligand of the peroxisome proliferator activated receptor alpha (PPARα). Activation of this receptor has analgesic and anti-inflammatory properties. In this study, we investigated the downstream consequences of PPARα activation and how this led to modulation of the inflammatory processes. Intra plantar subcutaneous (s.c) injection of 2% (v/v) λ- carrageenan (100 µl) into the rat hind paw (Sprague Dawley, male, 200-225 g) significantly altered hind-limb weight bearing and increased paw volume consistent with hyperalgesia and inflammation. Pre-treatment with PEA (50µg/50µl, s.c) 30 minutes pre-carrageenan significantly delayed the onset of hyperalgesia, but not the increased oedema for 2 hours. Post-mortem plantar skin samples were used in Taqman Low Density Arrays (TLDA) mRNA for 83 genes associated with inflammation. Results revealed PEA able to inhibit some of important pro-inflammatory chemokines that associated with immune cells recruitment which upregulated by TLR4 ligand-carrageenan. In immunofluorescence analysis, it further confirms the anti-inflammatory mechanism of PEA where it significantly inhibited the infiltration of monocytes into the skin but not the neutrophil numbers.

In vitro, PEA and synthetic PPARα agonist GW7647 significantly inhibited the LPS-stimulated differentiation of monocytes into macrophages which subsequently led to the selective inhibition of the secretion of specific chemokine that are known to promote the recruitment of monocytes/macrophages but not neutrophils. This study provides a new understanding of the mechanism by which PEA differentially modulates TLR4- mediated signalling pathways and consequent inflammatory responses.

Keywords: Lipid mediator, TLR-4, PPARα, Inflammation, Pain, Macrophages

ONPIM-24

Effectiveness of red palm oil in preventing alzheimer's disease induced in rat

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Age has a significant impact on neurodegenerative disease vulnerability. During aging, the level of oxidative stress is increasing that causes damage to the neurons, mitochondria, protein and DNA. Hence, brain aging has become a major risk factor for the development of neurodegenerative brain disorders such as Alzheimer's disease and Parkinson disease. This study was carried out to determine the effectiveness of red palm oil (RPO) in preventing brain aging induced in rats as RPO is known as a natural source rich with antioxidant properties. Forty male *Sprague-Dawley* rats were divided into 5 groups (n=8) that comprised normal group (saline water), negative control (D-Galactose, 100mg/kg), two treatment groups that were administered by RPO daily (200 and 400 mg/kg) and Donepezil, (0.25mg/kg) were given as positive control for 21-days. Y-maze spontaneous alternation test was done weekly to evaluate the spatial working memory of the rats. Last day of treatment, biomarkers of oxidative stress such as GSH, SOD and neurotransmitter biomarkers, dopamine in the blood, were measured through Elisa. Rats treated with RPO showed significant improvement in exploring new areas as compared to untreated rats ($p<0.05$). On the other hand, current results showed high levels of dopamine and GSH in rats treated with RPO and donepezil compared to D-Galactose induced rats after 21 days of pre-treatment ($p<0.05$). Meanwhile, total SOD was increased in all groups that were induced with D-Galactose. Overall, RPO has been proven to improve cognitive impairment in rats with brain aging. This is owing to the antioxidant properties of RPO which play a vital role in preventing oxidative stress. In the future, RPO could appear as a novel therapeutic molecule for brain disease.

Keywords: Oxidative stress, Brain aging, Antioxidants, Red palm oil

ONPIM-26

Giving new birth to synbiotics as pharmaceutical carrier beyond their use as nutraceuticals: Case studies

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Synbiotics have gained much attention in the current era and are considered as a new platform for management of different diseases. Several works have proven their potential for treating diseases such as diabetes, cancer, cardiovascular diseases and oxidative stress. However, for the first time the other face of synbiotics i.e. as a solid carrier was explored owing to their amorphous nature. In one study the liquid self-nano emulsifying drug delivery system was formulated and converted into free-flowing powder using the synbiotics having combination of *Ganoderma lucidum* mushroom polysaccharide and Biomix-1 (probiotics). The solid powder was further spray dried and converted into pellets. Similarly in another study the same combination of synbiotics was used as a carrier for the solidification of liquisolid compacts loaded with quercetin. Prepared formulations showed very good flow rate, angle of repose and compaction properties. The release was found more than 90% in 5 min from both the formulations whereas less than 20% drug release in 60 min was observed from raw drugs. Similarly, significant improvement in permeability was observed from formulations using caco2 cell lines. The non-significant difference in drug loading, droplet size, dissolution rate and angle of repose indicated the potential of synbiotics to produce stable solid formulations. Based on the positive outcomes of these two studies it was concluded that synbiotics can be explored further for solidification of other drug delivery systems wherein they can offer therapeutic benefits as well as pharmaceutical carrier potential and minimize the use of synthetic solid carriers such as Aerosil-200.

Keywords: Synbiotics, Solid carriers, Dissolution, Curcumin

ONPIM-27

In silico analysis of *Houttuynia cordata* active compounds against SARS-Cov-2 Mpro and helicase

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SARS-CoV-2, the virus responsible for COVID-19 pandemic has been shown to have a high mutation rate. This will increase the ability of the virus to escape natural or vaccine-induced immunity. Therapeutics targeting SARS-CoV-2 RNA synthesis and replication will play a crucial role in the development of multi-targeted treatment options for COVID-19. Previously, *Houttuynia cordata* (HC) plant extracts exhibited immunomodulatory and anti-SARS activities. Therefore, this study evaluated the binding interactions of HC active compounds on SARS-CoV-2 Main protease (Mpro) and helicase using molecular docking approach. A total of 20 selected HC active compounds were docked against SARS-CoV-2 Mpro and helicase using Autodock 4.2.6. The compounds with most populated cluster and lowest binding energy conformation were selected and further analysed on the binding interactions. Kaempferol, Afzelin and Isoquercitrin were found as the three most potential compounds against SARS-CoV-2 Mpro with the binding free energy of -8.64, -8.58 and -7.87 kcal/mol respectively. Meanwhile, Cepharadione B, Quercitrin and Cepharanone B were the three compounds that showed the highest binding affinity against SARS-CoV-2 helicase with the binding free energy of -6.85, -6.85 and -6.50 kcal/mol, respectively. The interaction analysis showed that formation of hydrogen bonding network and hydrophobics interaction were the major contribution in the binding interaction of all six compounds against both Mpro and helicase. In conclusion, this study had identified six *Houttuynia cordata* compounds which may potentially interact with SARS-CoV-2 Mpro and helicase, and therefore worthy for further evaluation using *in vitro* and *in vivo* assays to determine their potential as COVID-19 treatment.

Keywords: SARS-CoV-2, COVID-19, *Houttuynia cordata*, Antiviral, Main protease (Mpro), helicase, Molecular docking

ONPIM-28

Subacute oral toxicity study of epigallocatechin-3-gallate in Spontaneously Hypertensive Rats

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Epigallocatechin-3-gallate (EGCG) has been frequently promoted as a cardioprotective agent, however, there is still lack of scientific evidence on the safety profile of EGCG on cardiovascular disease model. This study aims to examine the potential subacute toxic effect of oral EGCG in Spontaneously Hypertensive Rats (SHR). Oral EGCG at 50, 250, 500 or 1000 mg/kg *b.w* were given to 12-week-old SHR for 28 days. Observation of the behavioural and general toxicity was conducted in accordance with the OECD 407 Guidelines. General condition and changes in skin, fur, eyes, movement and posture, appetite, defecation, urination and respiration, response to handling, grooming and locomotive patterns were monitored. At the end of the experiment, thoracic and abdominal organs were observed for gross lesion, changes in weight and external appearance. There were no changes in water and food intake in EGCG treated group. In general, there were no changes in weight gain, except in SHR treated with 500 mg/kg *b.w* of EGCG, in which this group showed a lower weight gain compared to untreated SHR. None of the rats died, showed abnormal behaviour or any clinical signs. There were no changes in gross anatomy and relation organ weight of the thoracic and abdominal organs observed. In conclusion, oral EGCG for 28 days up to 1000 mg/kg *b.w* does not cause significant toxic effects in SHR. Nevertheless, due to its considerable pro-oxidative activity and indications of EGCG-induced organ damage, more pre-clinical and clinical studies are required to establish the safety profile of EGCG.

Keywords: EGCG, Catechin, Green tea extract, Spontaneously Hypertensive Rats, Toxicity

ONPIM-29

Variability in pain tolerance after administration of standardized kratom decoction

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Kratom, or Ketum in Malaysia has a long history of folk medicine use in Southeast Asia and recently has gained popularity in Western countries. Mitragynine (MG) is the principal alkaloid reported to be responsible for Kratom's therapeutic actions. Pain relief is among many self-reported beneficial kratom effects. However, there are no controlled clinical studies reporting the analgesic property of Kratom employed as standardized formulation. The objective of this study was to scientifically assess the variability of the pain relief effects of Kratom decoction in a randomized, double-blind, placebo-controlled study. Kratom and placebo decoctions were prepared and standardized as a formulation to be administered to the subjects in the clinical study. Twenty-six Malaysian males (chronic Kratom users), mean (SD) age 24$\pm$3 years, participated in this study. Both Kratom decoction and placebo were matched for tastes and appearances. Pain tolerance was measured objectively using a cold pressor task (CPT). Both HPLC-DAD and LCMS/MS methods were validated and successfully applied to quantify mitragynine in Kratom decoction and plasma respectively. Pharmacokinetic and pharmacodynamic modeling were performed. The current study found out that there was no significant relationship between the mitragynine plasma concentration and pain tolerance; conceivably due to small sample size, large variation in the body weight and kratom consumption, with the high baseline level of mitragynine in plasma. The role of other alkaloids in Kratom may also be responsible to modulate the pain responses. Future studies on the effect of other alkaloids could help to establish their role in pain tolerance.

Keywords: Kratom, Mitragynine, Decoction, Pain Tolerance, Variability

ONPIM-30

An insight into cholesterol- reducing and Bile Salt Hydrolase (BSH) activity of *Lactobacillus spp.* as a potential probiotic bacteria

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Species of the genera Lactobacillus is among the lactic acid bacteria most commonly applied in industry due to their important roles as starters in healthy fermented foods. A total of 228 samples received in the form of glycerol stocks were revived on MRS agar plates for phenotype identification. The respective colonies were subjected to Gram stain, catalase and oxidase test. Further identification was carried out via molecular means. Biochemical tests for probiotic properties included bile salt tolerance, acid tolerance, bile salt hydrolase (BSH) activity and cholesterol assimilation tests. Out of 228 samples, only 34 isolates phenotypically identified as Lactobacillus. Primers Lac1 and Lac2 were used for 16S rRNA gene amplification which then generated 231 base pair PCR products. bsh gene was identified using primer pair bsh1 and bsh2 that resulted in amplification of 104 base pair PCR products. Twelve out of 34 samples showed bands for bsh gene. These samples were further examined and were observed to have good ability to withstand the exposure to 0.3% bile salts for 3 h, with the highest resistance rate of 89.31% and showed good capacity to survive under low pH condition with the highest survival rate noted at 90.14%. They also displayed BSH activity and ability to assimilate cholesterol to different levels. In conclusion, the current study has successfully identified several Lactobacillus spp. isolates with potential as

probiotic strains. Furthermore, this project provides an important opportunity to advance the understanding and make an important contribution to the field of food biotechnology.

Keywords: Lactobacillus, Probiotic, Animal milk, Bile salt hydrolase, bsh gene

ONPIM-31

Metabolomics guided insights on the clinical pharmacology of *Andrographis paniculata* 1000mg in urine samples

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Metabolomics is an emerging technology guide to investigate the clinical pharmacology of phytomedicines. *Andrographis paniculate* (AP) is a phytomedicine that contained various terpenoid compounds include andrographolide, neoandrographolide, dehydroandrographolide and others. In clinical pharmacology, targeted metabolomics potential measures the metabolome of phytoconstituents that absorbed into human circulation while untargeted metabolomic could observed the human metabolites changes to predict phytomedicine perturbation. This study aims to explore the pharmacology effects of marketed AP capsules using untargeted metabolomics. The study is registered in ClinicalTrials.gov with identifier NCT04161404. Healthy volunteers were given AP 1000mg capsules under fasting condition. Pre-dose and three post-dose urine samples from six subjects were collected to analyze using Liquid Chromatography Mass Spectrometry Quadrupole Time-of-Flight with C-18 column and modified METLIN untargeted analysis method. Pool quality control samples and internal standards were applied during the analysis. The chromatograms were processed using MetaboAnalyst software. The data processing involved normalization, batch correction, principal component analysis, paired statistical analysis between pre-dose and post dose samples and mass spectrometry

peaks-to-spectra module to predict the human metabolic pathways using mummichog algorithm based on the Kyoto Encyclopedia of Genes and Genome (KEGG) library. Pentose and glucuronate interconversions, caffeine metabolism, tyrosine metabolism, D-Glutamine and D-glutamate metabolism significantly found in enrichment analysis between pre-dose and 4 hours post-dose. Ubiquinone and other terpenoid-quinone biosynthesis also observed which show the phytochemicals were absorbed into human circulatory system. Untargeted metabolomic using LCMS provides broad insights in investigation pharmacological effects of multicomponent phytomedicines.

Keywords: *Andrographis paniculata*, Untargeted metabolomics, Clinical trial, Liquid Chromatography Mass Spectrometry, KEGG

ONPIM-33

Preliminary *in vitro* assessment of potential probiotic of lactic acid bacteria isolated from local fermented foods & dairy products

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Probiotic refers to living microorganisms that contribute to better health quality of the host when being supplemented in an appropriate amount. The study aimed to evaluate and compare the probiotic potential and safety of lactic acid bacteria (LAB) strains isolated from local fermented foods and dairy products as key features for future industrial applications. Local fermented (belacan, tapay, pickled fish, beancurd and taucu) and dairy (goat milk and sour cream) products were serially diluted and spread plated on MRS medium. The isolated strains were identified by phenotypic and biochemical methods. Their probiotic characteristics (growth capabilities, antimicrobial activity, pH, NaCl and temperature tolerances) and safety properties (antibiotic resistance and hemolytic activity) were evaluated. Among the samples, ten LAB strains were isolated, six (6/10) isolates with best growing capabilities were preliminary selected for further potential probiotic characterization. All six isolates showed versatile carbohydrate metabolisms (glucose, fructose maltose and sucrose), homofermentative, catalase negative and identified as cocci (n=2) and bacilli (n=4). The results demonstrated that all six isolates were good acid (pH3-6), NaCl (2-8%) and temperature (4-37°C) tolerant and exhibited antibacterial activity against Gram-positive and -negative pathogenic bacteria. Upon assessment of their safety, these six strains were displayed non-hemolytic activity and sensitivity to the tested antibiotics (ampicillin, amoxicillin, erythromycin, chloramphenicol and penicillin). This study revealed that LAB isolated from local fermented and dairy foods, especially LAB strains

from pickled fish, exhibited desirable probiotic properties and have great potential for industrial applications to promote human and animal health.

Keywords: Probiotic properties, Lactic acid bacteria, Fermented foods, Dairy products, characterization

ONIM-35

Effects of polyphenol-rich traditional herbal teas on obesity and oxidative stress in rats fed a high-fat-sugar diet

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The present research work investigates the reduction in weight gain potential of polyphenol rich extracts of *Hibiscus rosa-sinensis* (HRS) and *Zingiber officinalis* (ZO) teas in high-fat-sugar diet-induced obese rats. Three herbal teas were prepared from HRS flowers and ZO rhizomes and their mixture (HRS:ZO, 3:1). Extracts were prepared and total reduced capacity (TRC) and total flavonoid contents (TFC) of the extracts were estimated as gallic acid and catechin equivalents (GAE and CE), respectively. TRC of HRS and ZO extracts were found to be 5.82 and 1.45 mg/g of dry plant material, measured as GAE while TFC were 9.17 and 1.95 mg/g of dry plant material, as CE, respectively. Reverse Phase-HPLC analysis revealed the presence of 15 phenolic acids and 4 flavonoids in herbal extracts of both samples. Catechin, rutin, gallic acid, 4-hydroxy benzoic acid, chlorogenic acid, caffeic acid and salicylic acid were the major compounds detected. 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay was performed and both extracts showed > 50% DPPH radical scavenging capacity. Two doses (250 and 500 mg/kg BW) of each tea were selected to assess anti-obesity potential using high-fat-sugar-diet-induced obesity model in Wistar Kyoto rats. Data showed that higher dose of HRS significantly reduced the body weight and body mass index in comparison to high-fat-sugar diet group. Total cholesterol, high- and low-density lipoproteins, triglycerides, kidney, liver and atherogenic indexes, bilirubin, aspartate aminotransferase, alanine aminotransferase, alkaline phosphate and serum creatinine of rats showed that HRS extract showed significant anti-obesity potential. Moreover, HRS extract also prevented the alterations in malondialdehyde, superoxide dismutase and reduced glutathione levels of treated rats, thus showed potential anti-oxidant effect. It is evident from the results that higher dose of HRS exhibited better

reduction in weight gain and *in vivo* anti-oxidant effect while ZO showed fewer protective effects.

Keywords: Nutraceutical, Obesity, Cholesterol, Kidney Index, High fat diet, Phenolic acids and flavonoids

ONPIM-36

Analyzing single nucleotide polymorphism (Gly >Ser) of GRIA1 gene in schizophrenia concerning Pakistani population

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Schizophrenia is a mental disorder and about 1.5% of the population of Pakistan suffers from schizophrenia. The etiology of schizophrenia is still unknown, but it could be stated that genetics and environmental factors play a significant role. The neurobiology of schizophrenia also involves the Impairment of glutamatergic neurotransmission. Therefore, Glutamate Ionotropic Receptor AMPA Type Subunit 1 (GRIA 1) could be considered a substantial contributor in causing schizophrenia. It maps at 5q33, which is a susceptible locus for schizophrenia as per three independent genome-wide scans. The aim of this study was therefore to investigate whether single nucleotide polymorphism (rs1127386, G/A) of GRIA1 is a risk factor for schizophrenia in the population of Pakistan. Schizophrenia cases (50) were recruited as per DSMV criteria, and 50 controls were recruited. Genomic DNA was extracted from blood and polymorphism was detected using ARMS (amplification refractory mutation system) PCR. The results were observed using Agarose Gel Electrophoresis. In control group 3.9% individuals were detected as wildtype homozygous (GG) whereas rest 96.1% individuals were heterozygous (AG). Whereas in cases, 4% were detected as wild type homozygous and 96% as heterozygous. No homozygous mutant (AA) was observed in either cases or control group. No obvious difference was found in the genotype distribution of cases and control. A multi-center study with large sample size is encouraged in the future to detect reliable association of this genetic polymorphism of GRIA1 in the schizophrenia patients of Pakistan.

Keywords: Schizophrenia, Genotyping, Glutamate Receptor, GRIA, ARMS PCR

ONPIM-37

Emulsified annatto tocotrienol reversed ovariectomised-induced osteoporosis in rats by downregulating sclerostin level

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Self-emulsified formulation has been demonstrated to improve the bioavailability and skeletal effects of annatto tocotrienol in ovariectomised rats, but the fundamental mechanistic question of how emulsified annatto tocotrienol prevent osteoporosis remained unsolved. This study aimed to explore the effects of self-emulsified annatto tocotrienol on the skeletal histomorphometric parameters and bone remodelling peptides in rats with osteoporosis due to ovariectomy (OVX). Eight-month-old female rats were randomised into 6 groups. The baseline was euthanised upon arrival. The ovaries of the sham were not removed. Ovariectomy was performed on 4 other groups. All rats were rested for 2 months for bone loss to develop. Subsequently, the OVX groups were given blank emulsifier, unformulated annatto tocotrienol (60 mg/kg/day), emulsified annatto tocotrienol (60 mg/kg/day) or raloxifene (1 mg/kg/day) orally for 2 months. The sham was also given blank emulsifier during this time. All rats were sacrificed after the treatment period. Bone histomorphometry was performed on the femur, while bone remodelling peptide level in the lumbar bone was measured using multiplex immunoassay. All rats treated with annatto tocotrienol showed improvement in trabecular bone volume, osteoblast number and mineralisation rate compared to the untreated OVX rats ($p<0.05$). The sclerostin level was lower in annatto tocotrienol treated rats than in untreated OVX rats ($p<0.05$). The raloxifene group showed similar changes as the annatto tocotrienol-treated rats. In conclusion, emulsified annatto tocotrienol reverse osteoporosis due to oestrogen deficiency by suppressing sclerostin level in rats.

Keywords: Bone, Osteocytes, Osteopenia, Menopause, Vitamin E

ONPIM-38

Mango seed copper oxide nanoparticles: Preparation and application

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Nanoparticles are a large class of matter less than 100 nm in size, shapes, and various applications such as drug delivery, chemical, and biological sensing. However, copper oxide nanoparticles are also widely used for diverse purposes like antibacterial activities, gas sensing, high-temperature superconductor, etc. The polysaccharide extracted from different sources used in making polysaccharide nanoparticles in our research were mango seed nanoparticles. Mango seeds are the cheapest source of polysaccharides and are easily available in Pakistan. Our primary purpose was to prepare mango seed copper oxide nanoparticles through a two-step process: First, CuO nanoparticles have produced using copper sulphate penta hydrate with the addition of ascorbic acid as a reducing agent extracted from lemon juice. Second, the capping of CuO nanoparticles with polysaccharides extracted from mango seeds was done by preparing samples with different ratios of polysaccharide and CuO added with citric acid. The CuO nanoparticles prepared by forming three samples 1, 2, 3 with different ascorbic acid quantities added; the three samples gave 0.414g, 0.7127g, and 0.7150 g, respectively. The results show copper oxide yield changes with vitamin c level and its UV vis spectra show its peak absorption is in agreement with the previous published research, while of polysaccharide copper oxide nanoparticles shows that a bond has been established between CuO and polysaccharide and polysaccharide absorption increase when it is attached with metal nanoparticles.

Keywords: Mango Seed, Copper oxide Nanoparticle, Polysaccharide

ONPIM-39

Bioenhanced tocotrienol-rich vitamin E (Tocovid) improves nerve conduction velocity in type 2 diabetes mellitus patients in a phase II double-blind, randomized controlled clinical trial

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This study aims to investigate the effects of bioenhanced tocotrienol-rich vitamin E (Tocovid SuprabioTM) on nerve conduction parameters and serum biomarkers among type 2 diabetes mellitus patients. Eighty-eight patients were randomized to receive 200 mg of tocotrienol-rich vitamin E (Tocovid) twice daily or matching placebo for 12 months. Nerve conduction parameters, vitamin E levels and serum biomarkers were measured at 2, 6 and 12 months. After 12 months, patients in the Tocovid group showed highly significant improvement in conduction velocity (CV) of both median and sural sensory nerves compared to placebo. The between intervention group differences (treatment effect) in CV were 1.60 m/s (95% CI: 0.70, 2.40, p = 0.007) for median nerve and 1.97 m/s (95% CI: 1.10, 3.45, p = 0.036) for sural nerve. Significant improvement in CV was only observed up to six months in tibial motor nerve CV, 1.30 m/s (95% CI: 0.60, 2.20, $p < 0.001$). There were no significant changes in transforming growth factor beta-1 (TGFβ-1) and vascular endothelial growth factor A (VEGF-A). After six months of washout, there were no significant differences from baseline between groups in all nerve conduction parameters of all three nerves. Tocovid at 400 mg/day significantly improved median and sural sensory nerve CV at 12 months but improvement in tibial motor nerve CV was only observed up to six months. All improvements diminished after six months of washout.

Keywords: Vitamin E, Tocovid, Type 2 diabetes mellitus, Nerve conduction, TGF-β1, VEGF-A

PNPIM-02

Atrophic vaginitis by gelam honey in Sprague Dawley rats: Pilot study of potential apitherapy for managing genitourinary syndrome

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Atrophic vaginitis (AV) is a major response to hypoestrogenicity, a deprivation of oestrogen characteristic of genitourinary syndrome amidst developing menopause. Alternative hormone replacement therapy (HRT) is extensively being developed from substitute natural sources for women ineligible to receive HRT due to history of breast and or gynaecologic cancer, cardiovascular and hepatic disease. Malaysia's Gelam honey (GH), sourced by *Apis dorsata* bees from flowers of Melaleuca sp. is a prized natural product that holds potential as apitherapy to manage AV. Apitherapy is an alternative branch of medicine using honey bee products including honey. The current pilot study aims to provide evidence for the efficacy of GH in augmenting atrophic vaginitis by enumerating the effect of GH on AV. GH, with its proven antioxidant and anti-inflammatory properties was administered to 16 sexually mature female Sprague Dawley rats divided into 4 groups. Rats were fed daily with GH using oral gavage at doses of 0.1, 1, 2 and 8 g/kg bw for two weeks. The oestrogenic properties of GH were investigated by measuring the resulting thickness of the vaginal epithelia and levels of serum oestradiol using ELISA following a two-week administration. In this study, GH administration increased mean thickness of the vaginal epithelial layer and level of serum oestradiol. Both parameters recorded the highest values in the group receiving 2g GH/kg bw. In conclusion, apitherapy using GH is possibly beneficial.

The oestrogenic effect holds potential for GH apitherapy to be considered as a potential component of managing genitourinary syndrome.

Keywords: Gelam honey, Apitherapy, Atrophic vaginitis, Vaginal epithelia, Serum oestradiol, Estrogen, Genitourinary syndrome, Menopause

PNPIM-03

A preliminary study of the effects of kelulut honey on ovarian histology in letrozole-induced polycystic ovary syndrome model in rats

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Polycystic ovary syndrome (PCOS) is the leading cause of anovulatory infertility. It is a combination of reproductive, endocrine, and metabolic diseases. Kelulut honey is stingless bee honey reported in many studies to benefit the metabolic, endocrine, and reproductive system. The present study investigated kelulut honey's effects on ovarian histology analysis in letrozole-induced PCOS in rats. 18 female Sprague Dawley (SD) rats weighing 120-150 g were divided randomly into six groups (n=3): including control (distilled water), PCOS induce (1 mg/kg letrozole), and four experimental PCOS groups. Rats were treated with letrozole for 21 days to induce PCOS. In experimental groups, PCOS rats were treated with three doses of Kelulut honey (0.5, 1, and 2mg/kg) or distilled water for 35 days. Treatment with 1 mg/kg Kelulut honey significantly increases the corpus luteum count in the ovary of PCOS-induced rats. PCOS induce group show the highest number of ovarian cyst and lowest number of corpus luteum. However, no significant changes were found in other ovarian histology analyses: antral follicles, atretic follicles among the different groups. In conclusion, kelulut honey showing potential in inducing ovulation assessed through increasing the count of corpus luteum.

Keywords: Polycystic Ovary Syndrome, Kelulut honey, Ovary histology, Anovulatory infertility, Stingless bee honey

PNPIM-04

Synergistic anti-inflammatory effect of *Vitex trifolia* leaves hydroalcoholic extract and diclofenac against LPS-induced RAW264.7 cells

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Inflammation is the immune system response to different types of stimulation from infection and tissue damage leading to the pathogenesis of several chronic diseases. Conventional drugs such as non-steroidal anti-inflammatory drugs (NSAIDs) possess deleterious side effects after prolong use. *Vitex trifolia* is a shrub (family Verbenaceae) traditionally used to treat inflammation-related disease in several Asian countries with potential anti-inflammatory effects. However, its synergistic effect with NSAIDs is yet to be investigated. This study aims to determine the synergistic anti-inflammatory effect of *V. trifolia* leaves hydroalcoholic extract (VT) with diclofenac against RAW264.7 cells induced with lipopolysaccharide (LPS). The levels of IL-1β, IL-6, TNF-α and COX were measured in the LPS-induced RAW 264.7 cells. The results showed, VT (50 and 100 µg/mL) and diclofenac (100 µg/mL) significantly ($p<0.05$) reduced the levels of TNF-α, IL-6, and COX compared to the cells treated with LPS (1 µg/mL) alone. Thus, the synergistic effect was observed with VT-diclofenac combination on LPS-induced IL-6 production. In conclusion, VT-diclofenac combination potentially exhibits enhanced anti-inflammatory properties via the inhibitory effects on inflammatory cytokines production and COX activity, *in vitro*. Further molecular investigations on the combination and *in vivo* studies are suggested for future works.

Keywords: *Vitex trifolia*, Diclofenac, Anti-inflammatory, RAW264.7, Lipopolysaccharide, Cytokines, Synergistic effect

PNPIM-05

GC-MS analysis of terpenoids from leaves of *Canarium odontophyllum* Miq. (DABAI)

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Terpenoids are defined as secondary metabolites with molecular structures containing carbon backbones made up of isoprene (2-methylbuta-1, 3-diene) units. They show significant pharmacological activities, such as antiviral, antibacterial, antimalarial, antiinflammatory, anticancer activities and inhibition of cholesterol synthesis. *Canarium odontophyllum* or locally known as "dabai" is an endemic plant in Sarawak, Malaysia. Its leaf compositions were examined by using the GC-MS analysis in order to determine the similarities and differences among their volatile terpenoids constituents. Terpenoids content were 36.67% and 14% for hexane and ethanol extracts respectively. n-Hexadecanoic acid, phytol and octadecanoic acid were the major terpenoids constituents of *C. odontophyllum* leaf. n-Hexadecanoic acid (20.22%), phytol (8.74%) and octadecanoic acid (7.54%) were found to be predominant in the hexane extract, while phytol (21.02%) and n-hexadecanoic acid (14.52%) were major constituents in ethanol extract. The *C. odontophyllum* leaf constituents are also related to their biological activities and would offer promising therapeutic effects. Further investigation should be conducted to develop it as a potential therapeutic drug.

Keywords: *Canarium odontophyllum*, Dabai, GC-MS, Terpenoids, n-hexadecanoic acid, Phytol, Octadecanoic acid

PNPIM-06

Sperm morphology and testis histological changes in 12% high cholesterol diet administered rats following tualang honey supplementation and diet modifications

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Hypercholesterolaemia is recognized as a factor associated with male infertility. However, currently, there is limited therapy available. Tualang honey (TH) is a type of Malaysian polyfloral wild honey produced by the rock bee (*Apis dorsata*) proven to exert both anti-inflammatory and anti-oxidative effects. This study aimed to determine the effects of TH coupled with diet modification on sperm morphology and testis histology of 12% high cholesterol diet (HCD) administered rats. Fifteen rats were fed with HCD for 16 weeks. They were then divided into 3 groups. Group A rats were not treated and continued HCD as control. Group B rats were supplemented with TH (3.0g/kg) and continued HCD, while group C was given TH (3.0g/kg) but was changed to a normal diet for 4 weeks. Group B and C demonstrated significant improvement in sperm morphology compared to group A ($p<0.001$). Group C (TH and diet modification) showed significant improvement in sperm morphology compared to Group B which was given only TH ($p<0.05$). However, there is no significant improvement in Johnsen testicular scoring. Diet modification in addition to TH supplementation may further improve male fertility in HCD rats as compared to TH alone. Based on our findings, there is a need to further explore the potential of TH in improving male infertility associated with hypercholesterolaemia.

Keywords: High cholesterol diet, Tualang honey, Sperm morphology, Testis histology, Johnsen testicular scoring

PNPIM-07

Polygonum minus reduces angiotensin converting enzyme and angiotensin II in human umbilical vein endothelial cells

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Hypertension is associated with oxidative stress and overactivation of the renin angiotensin system (RAS). Angiotensin converting enzyme (ACE) and angiotensin II (Ang II) are the key proteins in RAS which are involved in the regulation of blood pressure. *Polygonum minus* (PM) is a herb with antioxidative activity but its effects on ACE and Ang II have not been explored. Therefore, this study aimed to evaluate the potential antihypertensive activity of PM via its effect on ACE and Ang II levels *in vitro*. Human umbilical vein endothelial cells (HUVEC) were cultured and treated with phorbol 12-myristate 13-acetate (PMA) to induce ACE activity. The cells were concomitantly treated with standardized aqueous extract of PM leaf for 24 h. Then, the ACE and Ang II protein levels were determined via enzyme-linked immunosorbent assay. Treatment with PM alone did not cause a significant change in the ACE and Ang II levels compared with the control group. PMA significantly increased the levels of ACE (P <0.05) and Ang II (P <0.05). Treatment of PMA-induced HUVEC with PM successfully decreased ACE (P <0.05) and Ang II (P <0.05) protein levels. PM reduces ACE and Ang II levels in PMA-induced HUVEC, thus demonstrating its potential antihypertensive effect.

Keywords: Angiotensin II, Angiotensin converting enzyme, Human umbilical vein endothelial cells, Hypertension, *Polygonum minus*

PNPIM-08

Protective effects of DHA and tualang honey against oxidative stress induced by chronic stress in rat brain

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Exposure to chronic stress induces oxidative damage which alters the dynamic balance between antioxidant and pro-oxidant activities in the brain. Tualang honey (TH) is a Malaysian wild multifloral honey which has been shown to contain high amount antioxidants. Docosahexaenoic acid (DHA) a form of omega-3 fatty acid found in fish which has been shown to possesses some antioxidant activity. This study aimed to evaluate anti-stress activity of DHA TH and their combination on several parameters of oxidative stress in the rat brain. Fifty male Sprague Dawley rats were divided into (i) control, (ii) stress-exposed, (iii) stress-exposed and treated with TH (1 g/kg body weight twice daily), (iv) stress-exposed and treated with DHA- (450 mg/kg body weight twice daily), and (v) stress-exposed and treated with a combination of TH and DHA. The chronic stress regimen consisted of a combination of restraint stress and a swim stress test for consecutive 28 days. Our results indicated that both DHA and TH significantly ($p < 0.05$) caused significant increase in total antioxidant capacity and suppressed lipid peroxidation. For glutathione status, only TH and not DHA, significantly reduced stress-induced elevation of oxidised glutathione (GSSG). In all parameters, there was no significant difference between rats receiving combination of TH plus DHA compared to TH alone and DHA alone indicating combination of DHA and TH was not superior to consuming DHA and TH alone. In conclusion, both DHA and TH may have protective effects against brain oxidative stress induced by exposure to chronic stress.

Keywords: Oxidative stress, Honey, DHA, Omega-3, Restraint stress, Rat brain

PNPIM-09

Quantification of phenolics content and antioxidant properties of *in vitro* and conventional propagated leaves of *Clinacanthus nutans*

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Clinacanthus nutans is belongs to family Acanthaceae, locally known as Sabah Snake Grass and Belalai Gajah. *C. nutans* is an ethnomedicinal plant with wide range of bioactive compounds that responsible for numerous biological activities. Due to its beneficial values, this species has been overharvesting to fulfil the demand from pharmaceutical industry. The biotechnology approach is adapted to overcome the problem. *In vitro* technique is a well-founded technology, commonly used not only for large-scale production of plants, but also as a platform in the production of various types of bioactive compound. The leaves of *in vitro* and conventional propagated *C. nutans* at six weeks old were used to evaluate the phenolics and antioxidant properties using several *in vitro* antioxidant assays. From this study, the leaves of *in vitro* propagated were significantly produced the highest total polyphenols, phenolic acids, flavonoids content and antioxidant properties including DPPH, ABTS, FRAP and superoxide anion scavenging activity. As conclusion, the phenolics content and antioxidant activity produced by *in vitro* technique was comparable with conventional propagation technique. Hence, mass production of bioactive compounds can be produced via *in vitro* technique and conserve wild population of *C. nutans*.

Keywords: *Clinacanthus nutans, in vitro* propagation, Conventional propagation, Phenolic content, Antioxidant properties

PNPIM-10

Polygonum minus inhibits tumor necrosis factor-α-induced endothelial cell migration

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Angiogenesis is a process involved in neovascularization and has been found to be associated with diseases like atherosclerosis and cancer. Therefore, identification of anti-angiogenic agent is highly important. Cell migration is the first step in angiogenesis and it is mediated by chemoattractant such as basic fibroblast growth factor (bFGF). *Polygonum minus* leaf or "Kesum" as commonly known in Malaysia has been shown to have antioxidative, anti-inflammatory, anti-ulcer and antimicrobial activities. However, their anti-angiogenic effect has not been investigated. Hence, this study was carried out to determine the effect of standardized aqueous extract of *P. minus* leaf on migration and bFGF expression in tumor necrosis factor (TNF)-α-induced human umbilical vein endothelial cells (HUVEC). HUVEC were pre-treated with *P. minus* for 18 h followed by induction with TNF-α for 6 h. Subsequently, HUVEC migration was evaluated using scratch assay and the protein level of bFGF was determined by enzyme-linked immunosorbent assay. Induction with TNF-α enhanced HUVEC migration ($P < 0.001$) and increased bFGF level ($P < 0.0001$). Pre-treatment with *P. minus* significantly reduced HUVEC migration compared with the TNF-α group ($P < 0.0001$). However, *P.minus* did not decrease the level of bFGF in TNF-α-induced HUVEC. Hence, it is concluded that aqueous extract of *P.minus* leaf inhibits TNF-α-induced HUVEC

migration and this effect is not mediated by bFGF. Further studies are needed to elucidate the pathway that is involved in the inhibition of endothelial cell migration by *P.minus*.

Keywords: *Polygonum minus*, Angiogenesis, Human umbilical vein endothelial cells, Basic fibroblast growth factor, Tumor necrosis factor-α

PNPIM-11

Physico-chemical characterization of bilayer composite palm tree-based nanocellulose as a potential wound dressing

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The optimum aim for a wound to heal should serve a great impact on the quality of life. Thus, the production of an ideal wound dressing is widely on the track, to eliminate certain drawbacks, including to promote tissue regeneration and prevent a bacterial invasion. This study aimed to develop a bilayer composite bioscaffold from natural-based resources for wound dressing. The bilayer hybrid bioscaffold was fabricated out from the combination of ovine tendon collagen type I and palm tree-based nanocellulose. The bioscaffold was post-cross-linked with genipin. The physical characteristics were evaluated based on its microstructure, pore size, porosity, water-uptake, retention capacity followed by degradation behaviour and mechanical strength. The chemical analysis was performed by the energy-dispersive X-ray spectroscopy (EDX), Fourier transform infrared spectrophotometry (FTIR), and X-ray diffraction (XRD). Results showed a uniform interconnected porous structure with optimal pore size ranging between 90-140 μm, good porosity (> 75%) and high-water uptake capacity (>1500%). The degradation process was more than 7 days. Further analysis with EDX identified main elements of the bioscaffold containing carbon, nitrogen and oxygen. By FTIR, the functional groups of collagen type I (amide A, B, I, II, and III) and nanocellulose (pyranose ring) were reported thus confirming the presence of collagen and nanocellulose in the bilayer hybrid scaffold. The XRD showed a smooth wavy wavelength consistent with amorphous material of the scaffold. Incorporation of nanocellulose in the collagen has positive influence on mechanical properties with increase in Young's Modulus and tensile strength while decrease in extension

at break. In conclusion, the fabricated bilayer composite bioscaffold with appropriate physicochemical and mechanical properties has a high potential as a skin wound dressing.

Keywords: Bioscaffold, Palm tree-based nanocellulose, Physico-chemical, Wound dressing

PNPIM-12

The effect of curcumin on wound healing

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Wound is attributed as a loss of cellular, functional, and anatomical continuity of live tissues. Wound healing involves four phase which are haemostasis, inflammation, proliferation and remodelling. *Curcuma Longa* (Curcumin) is a traditional medicinal plant used as herbal medicine in many parts of the world. Curcumin shows anti-inflammatory, antioxidant, antimicrobial and wound healing properties. The purpose of study was to evaluate the effectiveness of curcumin on wound length against the incisional wound healing in rat. In this study 21 healthy male Sprague-Dawley rats were selected. A linear 4 cm longitudinal full-thickness wound (incisional wound) with a depth of 0.5 mm was made on the dorsal part of the rat. After incision, 2% curcumin cream was applied on the wound of the treatment group for 14 days. The healing was assessed by the measuring the wound length on day 2, 4, 6, 8, 10, 12 and 14 of all groups except normal control group using vernier calliper. The length of wound healing is calculated based on the percentage of healing formula. The study revealed that there was no significant difference in 2% curcumin cream in wound healing due to several limitations in the present study such as formulation of product, doses, method of calculation, method of inducing the wound and lack of histopathological studies. However, this does not conclude that curcumin has no effect on wound healing since there is various study that proved curcumin accelerates in wound healing.

Keywords: Curcumin, Curcumin cream, Wound healing

PNPIM-13

Total phenolics and flavonoids compositions using FTIR fingerprinting and *in vitro* antioxidant activities of *Cuscuta reflexa*

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The aim was to identify functional groups and antioxidant activity of the extract. Soxhlet extraction method was employed to extract phenolic compounds from Cuscuta reflexa (C. reflexa) stems. The effect of extraction time (1-4 h) and concentration of ethanol (45%, 60%, 75% and 90%) on the percentage of yield, total phenolic (TPC) and flavonoid content (TFC) was investigated. The functional groups of phenolic compounds were characterized by using Fourier Transform Infrared Spectrometry (FTIR). DPPH and ABTS•+ radical scavengers were used to evaluate antioxidant activity. Data showed the highest % of yield (10.22 $\pm$ 0.14 w/w), TPC (64.11 $\pm$ 0.17, mg GAE/g d.w.) and TFC (41.08 $\pm$ 0.34, mg QE/g d.w.) at 3 h with 75% ethanol. FTIR results revealed the presence of functional groups associated phenolic compounds. DPPH and ABTS•+ radical scavengers were showed very potent antioxidant activity with IC50 295.12$\pm$1.33 and 245.43$\pm$0.78 µg/mL. The plants extract contains phenolics and flavonoids groups which has potent antioxidant activities. The study suggested for further in vivo study to confirm its therapeutics efficacy.

Keywords: *Cuscuta reflexa*, Phenolic content, Flavonoid content, Antioxidant

PNPIM-14

Aloe vera gel formulation for wound dressing: Comparison of different polymers using factorial 2^3 design

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Different topical preparation containing antibacterials for healing wound infection are available in market. Antibiotics are highly effective in wound healing, however their side effects such as irritation and skin allergy reaction are troublesome to the body if absorbed it will cause systemic side effect. These drawbacks could be avoided if the therapy was switched from synthetic to a natural active ingredient like plant *Aloe Vera*. Eight gel samples with 23design different concentrations of 3 types of polymers HPMC (Hydroxy propyl methyl cellulose) CMC (Carboxy methyl cellulose) and Carbopol 940P, with fixed concentration for both the Aloe Vera extract and Fusidic acid drug used in this research. All gels were checked for pH in range 5-6. Dissolution test was carried for all gel formulations and the marketed product. Formulation showed sustained release effect. Gel 2, 3,7, and 8 showed cumulative of drug release of 92.84%, 93.37%, 97.75% and 95.80 % respectively after 4hr. This high percentage could be to the concentration of the polymer that gave the drug chance to be easily released from the formulations and this could be induced diffusion mechanism due to an effective therapeutic bioavailability of the drug. However, Gel 4, 5, and 6 show slightly less sustained release of 19.61%, 12.76% and 23.58% respectively.

The release of fusidic acid from optimized Gel 7 was compared to marketed formulation Fusidic acid (Fucidin). The amount of drug release through the cellulose membrane was more than 97 % and nearly 46 % for marketed. Aloe Vera can speed up healing by facilitating drug release. This novel formulation can be employed for making burn wound healing process more efficient

and extensively to better patient compliance. In situ gel could be used as a potential cost-effective wound dressing material

Key words: Polymers, Sustained release, Aloe Vera, Fusidic acid

PNPIM-15

Parkia speciosa hassk empty pod mitigates cardiomyocyte hypertrophy by decreasing oxidative stress in H9c2 cells

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Oxidative stress plays an important role in the development of cardiac hypertrophy. Many plants have been shown to possess protective effects against cardiac hypertrophy. *Parkia speciosa* empty pod extract was reported to have positive effects on cardiovascular organs. Based on the information, this study aimed to investigate the effects *Parkia speciosa* empty pod extract on angiotensin II (Ang II)-induced cardiomyocyte hypertrophy. H9c2 cardiomyocytes were divided into five groups, namely control, Ang II (600 nM), *P. speciosa* extract (50 µg/ml, PS), Ang II+PS, and Ang II+valsartan (20 µM, positive control). The cells were exposed to the respective agents concurrently according to the group for 24 h. After the incubation, it was noted that Ang II increased cell surface area, cellular reactive oxygen species level, NADPH oxidase activity and reduced superoxide dismutase activity. These detrimental effects of Ang II were significantly reversed by the treatment of the extract, which were comparable to that of the valsartan. In conclusion, Parkia speciosa empty pod extract is able to confer cardioprotective effects against Ang II-induced cardiomyocyte hypertrophy, possibly by mitigating cellular oxidative stress.

Keywords: *Parkia speciosa*, Cardiomyocyte hypertrophy, Oxidative stress, NADPH oxidase, Superoxide dismutase, Reactive oxygen species

PNPIM-16

Nootrophic effect of *Syzygium polyanthum* leaves extract in chronic cerebral hypoperfusion rat model via cholinergic restoration: A potential therapeutic agent for dementia

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Vascular dementia (VaD) is associated with the loss of cognitive function. The pharmacotherapy for dementia is cholinesterase inhibitors (ChEI). However, currently available ChEIs produce side effects. Therefore, new anti-cholinesterase agents are required for treating dementia. *In vitro* assays showed that *Syzygium polyanthum* leaves extract (SPLE) inhibit acetylcholinesterase (AChE) and butrylcholinesterase (BuChE) activities. Here, we evaluate the nootrophic effect of SPLE mediated via cholinergic system in chronic cerebral hypoperfusion (CCH) rat. Male SD rats were subjected to permanent bilateral occlusion of common carotid arteries (POBCCA) or sham groups. Automated open field test (AOFT) was conducted to examine motor and exploratory functions. Cognitive functions were evaluated using Novel object recognition (NOR) and Morris water maze (MWM) tests. At the end of the behavioural task, the brain was harvested to determine cholinesterase and choline acetyltransferase (ChAT) activities along with acetylcholine (ACh) level. The study revealed SPLE (100, 200 and 300 mg/kg) (i) improved both non-spatial and spatial memories in NOR and MWM test, respectively and (ii) increased the ACh and ChAT activities in the frontal cortex, hippocampus and cerebral cortex. Interestingly, the elevated AChE activity in the hippocampus was significantly inhibited by SPLE extract. In conclusion, SPLE executes its cognitive functions by restoration of cholinergic system. The findings support the therapeutic potential of SPLE in the treatment of VaD.

Keywords: Vascular dementia, *Syzygium polyanthum*, Chronic cerebral hypoperfusion, Acetylcholinesterase, Choline acetyltransferase, Acetylcholine

PNPIM-17

Effects of *trans*-resveratrol and RU-615 on steroid-treated human trabecular meshwork cells morphology and cytotoxicity

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Human trabecular meshwork cell (HTMC) regulates intraocular pressure (IOP), the main risk factor and the treatment target for glaucoma. In steroid-induced ocular hypertension (SIOH), IOP is raised due to the increased in outflow resistance that blocks this pathway. *Trans*-resveratrol (TR) is a dietary polyphenol with antioxidative and anti-inflammatory properties, whereas RU-615 is a heterocyclic aromatic organic compound with anti-microbial and anti-hypertensive activities. Both agents were shown to reduce the IOP of SIOH rat model, however, their mechanisms are yet to be elucidated. Steroid-treated HTMC has been used as an in vitro model of steroid-induced glaucoma and is useful to use in evaluating potential antiglaucoma agents' mechanisms of IOP lowering. Therefore, the concentration chosen must be safe to be used on HTMCs. Primary HTMCs were cultured until passage 5 and divided into 7 groups for the treatment with TR and RU-615 with or without dexamethasone for 3 days. All groups were observed for their morphology daily and subjected to MTS assay after the incubation period. The morphology of the group treated with dexamethasone alone were generally wide, large and flat with spindle-like shape. Between the two compounds, the morphology was almost similar except for the TR-treated group 12.5 μM alone showed more elongated appearance. There were no significant differences between the dexamethasone-treated group and those treated with TR and RU-615 with or without dexamethasone. HTMCs treated with TR 12.5 μM and RU-615 0.1 mM with or without dexamethasone 100 nM are safe and non-toxic to their viability. (250 words)

Keywords: Steroid-treated glaucoma, *Trans*-Resveratrol, RU-615, Human Trabecular Meshwork Cells, MTS assay

PNPIM-18

Effects of *trans*-resveratrol on fibronectin expression in dexamethasone-treated human trabecular meshwork cells

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Increased deposition of extracellular matrix (ECM) in trabecular meshwork is known to contribute to aqueous humor outflow resistance, causing elevated intraocular pressure (IOP) and may progress to glaucoma. Glaucoma is an irreversible blindness and treatment options only target to reduce the IOP. Fibronectin (FN) is the most abundant ECM in human trabecular meshwork (HTM). Steroid-treated HTM cell is commonly used as *in vitro* model of ocular hypertension. *Trans*-resveratrol (TR) is a natural compound with the ability to reduce the IOP in steroid-glaucoma model, the mechanisms however are yet to be investigated. Hence, this study aims to the effect of TR on FN expression in steroid-induced FN expression in HTM cells. HTM cells passage 5 were divided into 5 groups and incubated with (1) media only; (2) DMSO (0.1%); (3) dexamethasone (100 nM); (4) TR only (12.5 uM) and (5) dexamethasone and TR. After 1-week of incubation, MTS assay was performed to assess the cell viability in all groups and ELISA method was used to measure the FN expression. The were no significant differences in the cell viability between the 5 groups ($p>0.05$). FN expression was significantly higher in HTM cells treated with dexamethasone compared to cells incubated in media only ($p<0.05$). Adding TR 12.5uM to dexamethasone-treated HTM cells for 7 days

significantly reduced the FN expression ($p<0.01$). HTM cells treated with TR 12.5 uM with or without dexamethasone is safe and non-toxic. TR reduces the FN expression in steroid-treated HTM cells.

Keywords: Fibronectin, glaucoma, Human trabecular meshwork, Steroid-induced glaucoma, *trans*-resveratrol

PNPIM-19

Role of honey and *Nigella sativa* against COVID-19 (HNS-COVID-PK): A multi-center placebo-controlled randomized clinical trial in Pakistan

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Till-date no definitive treatment exists for Coronavirus Disease 2019 (COVID-19). Honey and Nigella sativa (HNS) have antiviral, antibacterial, anti-inflammatory, and immunomodulatory properties. We conducted a multicenter, placebo-controlled, randomized clinical trial at 4 centers in Pakistan. RT-PCR confirmed COVID-19 adults showing moderate or severe disease were enrolled in the study. Patients were randomly assigned in 1:1 ratio to receive either honey (1 g/Kg/day) and Nigella sativa seeds (80 mg/Kg/day) or placebo up-to 13 days along with standard care. The outcomes included symptom alleviation, viral clearance, and 30-day mortality in intention-to-treat population. Moderate (210) and severe (103) patients underwent randomization from April 30 to July 29, 2020. Among moderate cases, 107 were assigned to HNS whereas 103 to placebo group. For severe cases, 50 were given HNS, and 53 were given placebo. HNS resulted in ~50% reduction in time taken to alleviate symptoms as compared to placebo [Moderate (4 versus 7 days) P<0.0001 and severe (6 versus 13 days) P<0.0001]. HNS further led to a better clinical score on day 6 with normal activity resumption in 63.6% versus 10.9% among moderate cases (P<0.0001) and hospital discharge in 50% versus 2.8% in severe cases

(P<0.0001). In severe cases, mortality rate was four-fold lower in HNS group than placebo (4% versus 18.87%, P=0.029). No HNS-related adverse effects were observed. HNS significantly improved symptoms, viral clearance, and mortality in COVID-19 patients. Thus, it represents an affordable over the counter anti-COVID therapy. This trial was registered with ClinicalTrials.gov Identifier: **NCT04347382.**

Keywords: COVID-19, SARS-CoV-2, Honey, Nigella sativa, Black cumin, Randomized Controlled Trial

PNPIM-20

Microarray data analysis to identify differentially expressed genes and biological pathways associated with tualang honey supplementation in NASH animal model

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Tualang Honey (TH) is a multifloral jungle honey that has been shown to have anti-inflammatory and antioxidant properties. Thus, it has been proposed as a potential supplement in the management of non-alcoholic steatohepatitis (NASH). This study aimed to identify potential key genes and biological process associated with the therapeutic effects of TH in NASH animal model. Twenty Sprague Dawley rats were used in this experiment. Five rats were given standard commercial pellets throughout the experiment and acted as controls. Fifteen rats were subjected to the 12% high-cholesterol diet (HCD) for sixteen weeks to induce NASH. They were then divided into 3 groups, with each group receiving 3 different dosages of TH supplementation for four weeks. RNA was extracted from serum using RNeasy extraction kit (Qiagen) and microarray analysis was performed. A total of 3062 differentially expressed genes (DEGs) were identified including 2788 upregulated genes and 274 downregulated genes in all treated groups. There were 15 genes significantly upregulated including aldehyde dehydrogenase family, cytochrome P450 and nuclear transcription factor. Whilst, 13 genes were significantly downregulated such as apelin, interferon regulatory factor 2 and stearoyl-Coenzyme A. Following pathway enrichment analysis, 34 biological processes were significantly modified ($p < 0.05$). Among the pathways implicated in the effects of TH were those involved in the inflammatory response, lipid biosynthetic process and cholesterol metabolic process. The present

study demonstrated that the DEGs involved in the therapeutic effects of TH were enriched in several pathways and further validation is required to confirm their specific roles.

Keywords: Tualang honey, NASH, DEG, Microarray, Pathway analysis

PNPIM-21

Neuroprotective potential of *Lavandula angustifolia* essential oil

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*L*avender (*Lavandula angustifolia*) essential oil (LEO) is traditionally used in aromatherapy for cognition related disorders. It is also approved by the European Medicines Agency (EMA) as herbal medicine to relieve stress and anxiety. LEO contains many bioactive terpenes, such as linalool, linalyl acetate, ocimene, 1,8-cineole, lavandulol, terpinen-4-ol, lavandulyl acetate, caryophyllene, and sesquilavandulol. This work aims to explore the neuroprotection potential of LEO and its two major compounds, linalool and linalyl acetate, against selected Alzheimer's disease models. LEO was screened for its acetylcholinesterase inhibitory activity, neurite outgrowth promoting potential and neuroprotective effect against a scopolamine-induced cell model. The results showed that LEO has very mild anti-acetylcholinesterase and neuritogenic activities but a significant neuroprotective effect. Linalool and linalyl acetate were also found to be responsible for LEO's neuroprotective effect. In particular, linalool ameliorated the scopolamine-induced cell death by counteracting the increase of intracellular reactive oxygen species. The findings suggest that linalool and linalyl acetate are partly involved in the neuroprotective mechanism of LEO via an antioxidant pathway. However, further studies are needed to elucidate the involvement of other possible interplayed mechanisms.

In conclusion, this study has demonstrated the potential of LEO and its main constituents as an alternative therapy in oxidative stress-related diseases.

Keywords: Alzheimer's disease, Antioxidants, Cholinesterase inhibitors, Essential oil, Lamiaceae, Lavandula, Neuroprotection, Scopolamine

PNPIM-22

Effect of drying methods and ethanol ratios on antioxidant capacity and *in vitro* anti-diabetic activity of *Cynometra cauliflora* fruit

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Cynometra cauliflora L. or known as "Nam-nam" or "Buah katak puru" grown mainly in northern peninsular Malaysia are known for its high nutritional and medicinal values in treating several diseases and for health care maintenance. However, there was lack of scientific data focusing on the chemical composition and biological activities. The current study aims to evaluate the effects of drying method and ethanol ratios on antioxidant and *in vitro* antidiabetic activities of *C. cauliflora*'s fruit extracts. In this study, *C. cauliflora* was collected, washed, cut, and were subjected to two different types of drying which are oven drying (OD) and freeze drying (FD). Then, the dried sample were extracted with ethanol at different ratios (100%, 50% and 0%) and their antioxidants (TPC, TFC, FRAP assay, and DPPH assay) and *in-vitro* anti-diabetic activities (α-amylase and α-glucosidase inhibition assay) were determined. The results indicated that the ethanol ratios had significant effect on the antioxidant activities of *C. cauliflora* fruit. The freeze-dried samples extracted in 50% ethanol showed the highest TPC and TFC values (170.41$\pm$2.91 mg GAE/g and 61.94$\pm$2.07 g QE/100g of dry samples, respectively). In addition, the IC50 value of freeze-dried samples extracted in 50% ethanol exhibited the strongest scavenging activity (IC50 value: 60µg/ml) and the highest reducing power at 1319.04$\pm$6.73 mM Fe/g compared to other samples. On the other hand, *in-vitro* anti-diabetic assay was not affected by the drying techniques and ethanol ratios. The α-glucosidase inhibitory activity revealed that there was a significant difference between freeze-dried samples extracted in 50% and 100% ethanol with the IC50 values of 45.53$\pm$2.0896 µg/ml and 158.36$\pm$2.4626 µg/ml, respectively. Meanwhile, the IC50 value for 50% ethanolic oven-dried extracts is 73.19$\pm$4.9634 µg/ml. On the other hand, 50% ethanolic freeze-dried extracts for α-amylase inhibitory activity showed the

strongest inhibitory effects with IC50 value 46.25±11.0718 µg/ml. Therefore, the freeze-dried samples extracted in 50% ethanol is the most active extract with the highest antioxidant and antidiabetic activity. Further study could be conducted to profile the metabolites responsible for the bioactivity.

Keywords: Oven dry, Freeze-dry, Nam-nam, Antioxidant, Anti-diabetic

PNPIM-23

Renal protective effects of *Trigonella foenum-graceum* seeds on morphine withdrawal rats

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Morphine is widely used as drug for treating chronic pain in post-operative and cancer patients. Unfortunately, over time, prolong morphine use can cause nephrotoxicity due to elevated level of oxidative stress. *Trigonella-Foenum Graceum* (TFG) known as fenugreek is well known for its antioxidative properties. Therefore, this study is done to evaluate the renal protective effects of TFG on the morphine induced rats. Male *sprague dawley* rats were divided into 5 groups (n=8), where excluding the negative group, the other four groups (positive and treatment groups) were administrated intraperitoneally with increasing dosage of morphine from 2.5 mg/kg until 50.0 mg/kg for 7 consecutive days. TFG extract was given orally as a treatment with the dosage of 250 mg/kg, 500 mg/kg, 1000 mg/kg for 21 days. Upon rat dissection, the kidney weight was measured and the oxidative stress markers namely malondialdehyde (MDA), superoxide dismutase (SOD), total antioxidant capacity (TAC) and glutathione (GSH) were measured using ELISA. In morphine administered rats, the MDA level was significantly increased meanwhile the levels of SOD, TAC and GSH were significantly reduced as compared to normal rat ($p<0.05$). Besides that, morphine administered rats treated with TFG extract shown a significant reduced level of MDA and high levels of SOD, TAC and GSH when compared to rats which were not treated with TFG extract ($p<0.05$). Overall, TFG extract treatment reduced the oxidative stress in kidney. The nephroprotective effects of TFG extract could be due to inherent antioxidant and free-radical-scavenging activity.

Keywords: Morphine, Fenugreek, Oxidative stress, Trigonella-Foenum Graceum, Kidney

PNPIM-24

Naja nigricollis venom extracellular vesicles biological function and interactions

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Therapeutic properties have been characterized for a variety of animal venom components, largely proteins with a role in envenomation effects. Snake venoms are known to contain biological molecules such as metalloproteases, thrombin-like serine proteases, and phospholipases. Snake venoms have been characterized to carry extracellular vesicles which are a vehicle to transfer proteins, lipids and nucleic acids to recipient cells. EVs have been shown to participate in cell signaling and, in snake venoms, may contribute to the effects of envenomation. The black-necked spitting cobra (*Naja nigricollis*) venom is unusual to other elapids as it consists mainly of cytotoxins. The contents, interactions, and mechanism of action of EVs isolated from the venom of *N. nigricollis* were analysed with the aim of classification in a species for which these EVs have not been extensively described. Herein, we have analyzed the size and concentration of snake EVs from *N. nigricollis* by nanoparticle tracking analysis and electron microscopy. The properties and mechanism of action of snake EVs on mammalian cells was analyzed by cell proliferation, haemolysis and phospholipase 2 (PLA2) assays. Cellular uptake of EVs was followed by PKH67 staining of snake EVs into mammalian cells. EVs were found to inhibit cell growth with a different profile over time to whole venom suggesting an alternative mechanism of action. PLA2 concentrations were found to be higher in EV isolates than whole venom and haemolysis levels were comparable between EV and venom treatments. These results demonstrated that snake EVs may participate in envenomation effects and induce cell apoptosis through uptake and signaling mechanisms. This contributes to the understanding of *Naja nigricollis* venom and the profile of EV action in cell signaling and metabolic influence.

Keywords: Extracellular vesicles, Venom, Snake, *Naja nigricollis*, Envenomation

PNPIM-25

Elucidating the effectiveness of Red Palm Oil (RPO) in preventing Polycystic Ovarian Syndrome (PCOS) in rats

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RPO have many medicinal uses as they are rich in nutritional values. In a previous study, the nutritional content of the palm pollen showed a positive effect on improving PCOS. The current study is intended to identify the effect of RPO in improving induced PCOS in rats. Forty *Sprague Dawley* rats were divided into five experimental groups with eight rats in each group (n=8). This research intervention was carried out for 28 days. The rats in all groups except the control group were given 1 mg/kg of Letrozole diluted with 0.9% NaCl to induce PCOS. Positive control group was given 100mg/kg of Metformin dissolved in 0.9% NaCl. Intervention Group one and two were given 200mg/kg and 400mg/kg of RPO respectively. Negative group was only given Letrozole without any intervention. The Estrous cycle of the rats were monitored before and at the end of the research. The anxiety level of the rats was evaluated using the Elevated T-Maze test. After 28 days, the rats were sacrificed. The raw data of the research were analysed using SPSS (ANOVA)s. The BMI in the Intervention Groups were significantly lower compared to the negative group ($p<0.05$). Rats in intervention groups showed higher anxiety levels compared to control group and negative group ($p>0.05$). Estrous cycle of the rats in intervention groups was irregular compared to the control group ($p>0.05$). This study shows that RPO has the ability to improve only metabolic symptoms of the PCOS.

Keywords: PCOS, Red palm oil, Testosterone, Anxiety, Estrous cycle, BMI

PNPIM-26

Palm tocotrienol maintained the proliferation of MC3T3-E1 cells treated with dexamethasone

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Glucocorticoids are crucial for the induction of osteoblast differentiation and formation of a mineralized extracellular matrix. However, GCs excess causes decrease in bone mass and bone mineral density (BMD) and increase bone fracture risk. This is due to the dysfunction and apoptosis of osteoblasts and osteocytes and stimulation of osteoclast leading to suppression of bone formation and stimulation of bone resorption. MC3T3-E1 is the spontaneously immortalized murine calvarial cell line and widely used models of osteoblast biology. The aim of this study is to determine the effects of palm tocotrienol on the proliferation of the MC3T3-E1 cells treated with dexamethasone. Cells were seeded at 1x10^4 cells/well with culture media (Gibco MEM Alpha 10% FBS, 1% Antibacteria Antimycotic) in 96 well plate, triplicate, culture untill 80% confluent, treated with dexamethasone (LODEXA) 0, 50 and 150 uM and treated with Palm Tocotrienol (EVNOL) at the dose of 0.05, 0.1 and 0.5 ug/mL for 6 days. Cell proliferation assay was done, and the results were read using microplate reader at 490nm absorbance. Cell mineralization was quantified by Alizarin Red S staining. Results showed that dexamethasone at the dose 150 uM had significantly inhibited the proliferations of MC3T3-E1 and treatment with Palm Tocotrienol (EVNOL) at the dose of 0.5 ug/mL for 6 days significantly maintained the proliferation of MC3T3-E1. This strengthened the previous finding that palm tocotrienol protected the bone against dexamethasone by maintaining the osteoblast proliferation.

Keywords: MC3T3-E1 cells, Osteoblast, Palm tocotrienol, Proliferation, Dexamethasone

PNPIM 27

In vitro antibacterial screening and phytochemical profiling of Malaysian traditional plants used for treating diarrhea infection

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A total of 6 plants that are traditionally used to treat diarrhea infection were selected in this study. These include bark extract of *Erythrina variegate*, seed extract of *Mangifera indica*, leaf extract of *Murraya koenigii*, seed extract of *Quercus infectoria*, flower extract of *Syzygium aromaticum* and rhizome extract of *Zingiber officinale*. The *in vitro* antibacterial screening of the 80% methanolic extracts of the plants were determined using broth dilution method against 9 strains of diarrheal pathogenic bacteria that are *Escherichia coli* 0157:H7, *Vibrio alginolyticus* (ATCC 17749), *Vibrio parahaemolyticus* (ATCC 17082), *Salmonella paratyphi* (ATCC 9150), *Yersiniae enterocolitica* (ATCC 23715), *Listeria monocytogenes* (ATCC 19115), *Salmonella typhi* (ATCC 14028), *Escherichia coli* (ATCC 0157) and *Staphylococcus aureus* (ATCC 700699). The total phenolic content (TPC) was determined using Folin-Ciocalteu's (FC) method modified to the 96-well plate assay and the results were expressed as microgram of gallic acid equivalents per milligram extract (µg GAE/mg extract). Liquid chromatography with tandem mass spectrometry (LC-MS-MS) analysis was adopted for compound profiling of the leaf extract of *Murraya koenigii*. The least minimum inhibitory concentration value of 7.812 µg/ml was observed with the leaf extract of *Murraya koenigii*. The extract of *Zingiber officinale* possess the highest TPC of 445.22 µg GAE/mg. The LC-MS-MS analysis revealed the present of six (6) phytochemical compounds.

The compounds might be responsible for the inhibitory effect of the plant extracts. The results obtained from this study will provide new scientific evidence of the traditional uses of the plants in treating diarrhea infection.

Keywords: Traditional Malaysia plants, Diarrhea, Pathogenic bacteria, Broth dilution, Total phenolic content, LC-MS-MS, 80% methanol

PNPIM-28

Evaluation of antipyretic activity of roots extract of *Durio zibethiuns* on Wistar albino rats

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A fever is a body temperature that is higher than normal and it is not an illness. It is part of your body's defence against infection. Herbaldrugs can be used to treat many aliments, chronic and acute diseases and complications such as heartdisease, depression, inflammation and to increase the body defence. The aim of the study is to investigate the antipyretic activity of roots extract of *Durio zibethinus* on Wistaralbino rats. Dried pulverized roots were size reduced into coarse powder and subjected to cold maceration using ethanol for 10 days. Antipyreticactivity has been done by using brewer's yeast induced fever in albino rats. Rats were divided into five groups of six each. Group I as normal control, Group II as negative control, Group III received the standard drug Paracetamol (150mg/kg), Group IV received ethanolextract (200mg/kg/*p.o*) and Group V received ethanol extract (400mg/kg/*p.o*). Fever was induced using 20ml/kg (20%) Brewer's yeast suspension was injected subcutaneously at the back below the nape of the neck of the animals except the normal control group. The ethanol extracts at a low dose and high dose were subjected to access the antipyretic activity. Initial rectal temperature was recorded. Both doses of 200mg/kg and 400mg/kg was found to be significant in reducing rectal temperature. Higher dose showed better activity and significant ($P<0.01$) when compared to lower dose which is almost comparable to standard drug. However, the mode of antipyretic action of the extract have to be explored further to know the exact mechanism at molecular level.

Keywords: Paracetamol, *Durio zibethinus*, Antipyretic activity, Brewer's yeast, Wistar albino rats

PNPIM-29

Enhancement of *Phaleria macrocarpa* fruit extract on the male fertility tested in rats

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Phaleria macrocarpa has been claimed to improve sexual strength in man. Andropause occurs after middle age due to low testosterone level, affecting sexual strength and libido. The potential of the fruits for improving sexual strength in males has not yet been fully explored. A comparative study on the effects of fruits on the fertility in sixty Sprague Dawley adult male rats (7 weeks old) weighing 200-250g was conducted. A two by five experimental design with two supplementation periods (3 and 7 weeks) and 5 different doses of fruit extract (0, 24, 48, 240mg aqueous extract/kg bw and 80mg of commercia product/kg bw) were used. Body weight testes size and volume was measured. 3 mL of blood sample was collected from each rat via retro-orbital sinus bleeding procedures 24 hours after the last treatment for each treatment period for testosterone hormone analysis using radioimmunoassay technique. The results of the study were analyzed using SPSS showed that the mean testes size was similar ($p>0.05$) among treatment groups, ranging from 1.3 to 1.8cm. Forced feeding of the fruit extract produced no significant changed on the testosterone level, ranging from 1.03 to 1.42 ng/ ml while testes volume, remained at 2 mL throughout the study. Body weight was significantly highest ($p<0.05$) in rats treated with 240 mg/kg (301g), followed by 48 mg/kg (291g), 24 mg/kg (291g), commercial product (268g) and untreated rats (223g). The results showed that extract supplementation significantly increased the fertility of rats and the effect was dose and time dependent.

Keywords: *Phaleria macrocarpa*, Potency, Male, Testes, Testosterone, Weight

PNPIM-30

Bergenin protects hyperglycaemic induced testicular oxidative stress and revamp steroidogenesis in streptozotocin (STZ) induced type 2 diabetic rats

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Hyperglycaemia in DM is associated with increased risk of testicular dysfunction by stimulating oxidative stress while BG shown to alleviate it. Therefore, we hypothesized that BG could protect testes against hyperglycaemia-induced damage in DM. To induce DM, adult male SD rats were fed with high fat diet for 12 weeks followed by a low single dose of streptozotocin (STZ) intraperitoneally. DM was confirmed by checking FBG on third day post STZ injection. Oral treatment with BG started on the fourth day for 30 consecutive days at two doses (10 and 20 mg/kg/day) to the diabetic group. At the end of treatment, rats were sacrificed, and samples were immediately collected and preserved for molecular studies. Serum was separated from whole blood and epididymal sperms were collected for analysis. BG was found to reduce testicular oxidative stress MDA and inflammation by lowering the expression of inflammatory markers (TNF-α, NF-κB, IKKβ and IL-1β and iNOS) and improving endogenous antioxidant enzymes distribution (Nrf2, NQO1, HO1, SOD, CAT) in the testes of diabetic rats as compared to untreated diabetic control group. BG also shown to improve anti-apoptosis protein marker Bcl-2 and prevented upregulation of apoptosis marker caspase-3 and caspase-9 in the testicular tissue of diabetic rats. Moreover, BG also prevented the downregulation of testicular steroidogenic markers StAR, CYP11A1 and SHBG. Analysis of sperm parameter in the testes of diabetic rats treated with BG shows improvement

in viability, motility, and count. In conclusion, BG protects hyperglycaemic induced testicular damage and helps in maintaining testicular functions.

Keywords: Hyperglycaemia, Testicular dysfunction, Bergenin (BG), Oxidative stress, Inflammation, Apoptosis, Steroidogenesis

PNPIM-34

Ranuncoside reduced lipopolysaccharide-induced oxidative stress in postnatal mice: An *in vivo* study of neurodegeneration

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Persistent neuroinflammation is the major inducing cause of neurological disorders, including Alzheimer's diseases. The currently used pharmacotherapeutic agents are partially effective as they target and block one of the pathways only and offer mainly symptomatic relief. Therefore, there is an urgent need to explore additional therapeutic agents that target multiple molecules, which follows moving to one molecule multiple targets from mono-target pharmacology. Therefore, we isolated ranuncoside from *Ranunculus muricatus* and explored the therapeutic and mechanistic potential of ranuncoside against lipopolysaccharide (LPS) induced oxidative stress-mediated Aβ production and associated memory dysfunction in adult albino mice. LPS was administered intraperitoneally (IP) at 250 µg/kg/day for three weeks, followed by administration of ranuncoside at a dosage of 30 mg/kg/day for the last two weeks of the experiment. Western blot technique was used to assess the expression of different proteins involved in oxidative stress, neurodegeneration and neuronal synapse. The results indicate that ranuncoside significantly activated endogenous antioxidant proteins such as SIRT1, NF-κB and TNF-α compared to the control. Ranuncoside was successful to significantly reduce LPS induced apoptotic neurodegeneration, including BAX, Caspase-3, and PARP-1 proteins accompanied by inhibition of BACE1 and amyloidogenic pathway of Aβ production. Furthermore, ranuncoside improved both pre-neuronal and post-neuronal synapse and memory

dysfunction against LPS. Therefore, it is suggested that ranuncoside could be a suitable and prospective drug applicant in the management of neurotoxin triggered neurodegenerative disorders.

Keywords: Alzheimer's disease, Memory impairment, Neuroprotection, Neurodegenerative disease, Ranuncoside

PNPIM-35

Application of medicinal superfood and herb for versatile cancer management: A single-centre study

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Globally, a leading cause of death is cancer. The world witnessed approximately 18.1 million new cases and 9.5 million cancer-related deaths, which is expected to be increased to 29.5 million and 16.4 million, respectively, yearly by 2040. Unlike developed countries, developing countries like Bangladesh are more vulnerable due to poor healthcare, early diagnosis, lack of awareness, and inadequate treatment. Despite expensive treatment and the scarcity of trained professionals, adverse events of conventional treatment motivated researchers to find a better alternative. It is a common belief, and scientific evidence showed that natural remedies are safer than synthetic drugs. Therefore, this study evaluated the cancer management efficiency of different natural regimes practised in a personalized medical centre. Medicinal superfoods and herbs combinedly used to treat different tumours. We have found that combined decoction of *Christia vespertilionis*, *Ganoderma lucidium*, *Morinda citrifolia*, *Moringa oleifera*, *Nigella sativa*, flaxseed, soya, and the site-specific probiotic formulation was effective to recover early stages cancer patients, including breast, colorectal, prostate, cervical, ovarian cancer and different types of leukaemia and lymphoma patients. Tumour volume reduction, malignancies, vaginal discharge and improving the quality of life were positive signs of cancer management. Additionally, *in vitro*, *in vivo* and clinical studies' outcomes of these plants were assessed to validate the personalized treatment. The anticancer effects showed by inhibiting cancer-activating mutated genes and enzymes, stimulating DNA repairing mechanism, inducing cytotoxicity, antioxidant, regulating apoptosis and estrogen receptor signalling pathway. Routine diagnosis should be performed to confirm the anticancer efficacy of medicinal superfoods and herps.

Keywords: Anticancer agent, Cancer, Fruits, Quality life, Medicinal plant, Natural products

PNPIM-36

In vitro antibacterial and antibiofilm activities of essential oils from aromatic plants against human pathogenic bacteria

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The emergence of antimicrobial resistance bacteria leads to the discovery of essential oils (EOs) potentiality as an alternative approach to fight against certain bacterial infection. Therefore, the present study aimed to evaluate the antibacterial and antibiofilm activities of selected essential oils against human pathogenic bacteria. Total of five EOs extracted from aromatic plants were procured from local market and used in this study. They were *Syzygium aromaticum* (clove, CEO), *Eucalyptus globulus* (EGEO), *Pelargonium graveolens* (geranium, GEO), *Cymbopogon citratus* (lemongrass, LGEO) and Melaleuca alternifolia (Teatree, TTEO) essential oils. Their antibacterial activities against Gram-positive bacteria (*Staphylococcus aureus* and *Staphylococcus epidermidis*) and Gram-negative bacteria (*Escherichia coli* and *Klebsiella pneumoniae*) were assessed using agar disc diffusion along with broth microdilution methods to determine the minimum inhibitory concentrations (MICs) and minimum bactericidal concentrations (MBCs). The antibiofilm activities of all five EOs were evaluated by quantifying the biomass using the crystal violet staining method. All 5 EOs were exhibited antibacterial activities against all tested bacteria. CEO displayed significantly ($P<0.05$) higher antibacterial activity against all tested bacteria with largest inhibition zone (11.83-15.70mm) and lowest MIC (1.56-12.5µL/mL) and MBC (1.56-12.5µL/mL) values, as compared to other EOs. EGEO, TTEO, CEO, LGEO and GEO showed all tested bacteria biofilm inhibition up to 69.9, 80.1, 80.2, 85.8 and 87.7%, respectively, at 1-4×MICs. The eradication up to 39.4, 40.5, 60.7, 59.8 and 64.2% of the established biofilms of all tested bacteria were observed in GEO, LGEO, TTEO, EGEO and CEO, respectively, at concentration up to 4×MICs. The findings of

the present study highlighted that these five EOs could have potential role in the treatment of diseases related to infection by microorganisms.

Keywords: Antibacterial, Antibiofilm, Essential oils, Aromatic plants, Human pathogenic bacteria

PNPIM-37

Identification of a recurrent missense mutation in *SLC2A10* gene in arterial tortuosity syndrome patient in Saudi Arabia by next generation sequencing

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Arterial Tortuosity Syndrome (MIM # 208050) is an autosomal recessive and very rare genetic disorder characterized chiefly by tortuosity and elongation of arteries including both medium and large size, along with pulmonary arteries stenosis and the formation of aneurysm that lead to death in individuals in early years of life. Moreover, the other typical manifestation is often characterized by facial features and many connective tissue anomalies. So, in order to pursue our research, we recruited a patient with Arterial Tortuosity Syndrome, after evaluating clinically by pediatric cardiologist as well as clinical geneticists from King Abdulaziz University Hospital, Jeddah, Saudi Arabia. Peripheral blood was drawn and processed for genomic DNA extraction for further genetic analysis. We performed whole exome sequencing of the sample and found a homozygous missense mutation in exon 3 of *SLC2A10* gene where guanine is substituted by adenine at nucleotide position c.1309G>A leading to amino acid change from glutamine to lysine at position 437 (p.E437K). The segregation of this mutation was verified and found to be absent in unrelated healthy control subjects. Of note, our preliminary finding shows this causal mutation is autosomal recessive in nature. Interestingly, this mutation was previously reported in Italian patient in heterozygous form. Taken together our results indicate that this p.E437K mutation is being reported first time

in Saudi patient that lead to heavily perturb the GLUT10 function. However, studies with more samples should be performed to analyze the full spectrum of *SLC2A10* gene mutations in Saudi and other populations.

Keywords: Arterial Tortuosity Syndrome, *SLC2A10*, Congenital Heart Disease, GLUT10, p.E437K

PNPIM-38

Antioxidant properties of hot water extracts from *Crescentia cujete* leaf, bark, and fruit

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Crescentia cujete L., known as calabash tree, is commonly used in folk medicine to treat various types of diseases. The plant parts were typically boiled in water to extract the medicinal constituents. However, there is little information available on antioxidant activities and toxicity of hot water extracts from different parts of *C. cujete*. Therefore, the present study aimed to determine the antioxidant activities of hot water (HW) and 50% ethanol (ET) extracts of the leaves, bark, and fruit of the herb. The results showed that hot water extraction of *C. cujete* leaf exhibits the highest 2,2-diphenyl-1-picrylhydrazil (DPPH) radical scavenging activity with the highest antioxidant activity compared to all other plant parts of both solvent extracts. The IC50 of leaf extracts is 21.6 $\pm$ 0.11 µg extract/ml. The analysis of Ferric Reducing Power assay (FRAP) showed better reducing power in 50% ethanol extracts of fruit (43.723 $\pm$ 0.1 µmol Fe (II)/g DW) than other plant parts in both solvent extracts. The determination of the total phenolic content (TPC) using the Folin-Ciocalteu reagent showed that the bark extracted with 50% ethanol had the highest concentration of TPC (28.89 $\pm$ 2.05 GAE, mg/g) compared to solvent extracts of different plant parts. The estimation of total flavonoid content (TFC) using aluminium chloride assay showed hot water extracts of leaves contain a high amount of flavonoids compared to other plant parts of both solvent extracts (17.177 $\pm$ 0.984 QE mg/100g). Thus, it is indicated that hot water extracts of leaf exhibit excellent antioxidant activity and can be potentially developed as a functional food ingredient. Further in-vivo research and toxicity assessment could be conducted to validate the efficacy of the plant extracts.

Keyword: Antioxidants, Phenolics, Scavenging activity, *Crescentia cujete*, Flavonoids

PNPIM-39

Hypotensive effect of a partially purified fraction of *Gynura procumbens* in Spontaneously Hypertensive Rats

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Previous studies have demonstrated that a partially purified fraction (FA-I) of the *Gynura procumbens* leaf extract is able to inhibit the activity of the angiotensin-converting enzyme (ACE) *in vitro*. Inhibition of ACE is well-known for bringing about a decrease the blood pressure (BP) of an individual. In this study therefore, whether the fraction FA-I is able to decrease the BP accordingly in the spontaneously hypertensive rat (SHR), an animal model of hypertension, is investigated. Seventeen-week-old SHRs (n=6) and normotensive Wistar-Kyoto (WKY) rats (n=6) were given intravenous bolus administrations of 0, 0.625, 1.25, 2.5, 5 and 10 mg/kg of FA-I. The BP of rats was recorded via a direct and invasive BP monitoring technique onto a PowerLab data acquisition system and analysed with a LabChart 6 software. The hypotensive effect of FA-I was observed in SHR and WKY rats in a dose-dependent manner. However, FA-I significantly ($p < 0.05$) attenuated the mean arterial pressure (MAP) in the SHRs more than in the WKY rats, notably at the higher dose of 10 mg/kg ($p < 0.01$) FA-I does exert a hypotensive effect in the SHR rats possibly in part due to the presence of an ACE inhibitor.

Keywords: *Gynura procumbens*, FA-I, Hypotensive, Mean arterial pressure, Spontaneously Hypertensive Rats

PNPIM-40

Formulation development and characterization of liquisolid tablets of fisetin

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Fisetin is a plant derived flavonoid that possesses pharmacological activities like antioxidant, anti-inflammatory, hypolipidemic, anti-adipocyte differentiation, inhibition of allergic airway inflammation, neurotropic activity, anti-cancer and anti-depressant. Despite having various pharmacological properties, fisetin possesses low aqueous solubility and oral bioavailability. In the present study liquisolid formulation of fisetin has been reported with an aim to increase its dissolution rate. Initially, fisetin (20 mg) has been dissolved in 1 mL of tween-80 that served as liquid vehicle. The tween-80 solution containing fisetin was adsorbed on to the surface of aerosil-200 and directly compressed into tablets after blending the powder with MCC PH102 and PVP K-30. The tablets showed a significant increase in the dissolution profile as that of raw fisetin. More than 90% of drug got dissolved in the dissolution medium (0.1N HCl) in first 10 minutes, whereas, the naïve fisetin showed only 13% drug release in 60 minutes. The developed tablets were found stable for 6 months during accelerated stability studies carried at 40°C and 75% R.H. Overall, the study presented a simple and scalable approach to enhance the dissolution rate of lipophilic phytoconstituent fisetin via liquisolid technology.

Keywords: Dissolution, Fisetin, Liquisolid technology, Solubility

OND-01

Brain-derived neurotrophic factor attenuates amyloid beta 1-40 induced retinal injury and visual impairment in Sprague Dawley rats

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Amyloid beta (Aβ) deposition in the retina is associated with a loss of retinal ganglion cells (RGCs). Decreased levels of brain-derived neurotrophic factor (BDNF) are believed to be associated with the neurotoxic effects of Aβ peptide. This study aimed to investigate neuroprotective effects of BDNF against amyloid beta 1-40 peptide (Aβ1-40) induced retinal injury and visual impairments in *Sprague Dawley* rats. In this study, group 1 was intravitreally administered with PBS, group 2 was intravitreally administered Aβ1-40 (5 nmol/L), and group 3 was similarly co-administered with Aβ1-40 (5 nmol/L) and BDNF (1 µg/mL). Each group of rats were subjected to histopathological examination using H&E, Fluoro-Gold, Congo red and Toluidine blue staining, and TUNEL assay. Rats were also subjected to object recognition test and estimation of oxidative stress markers using ELISA. TrkB, ERK1/2, and caspase-3 expression at the gene and protein levels in retina was determined using RT-PCR and western blotting. In our study severe degenerative changes were observed in retina after intravitreal Aβ1-40 exposure. Fluoro-Gold staining showed a significantly lower count of RGCs in the Aβ1-40 group than in the control and BDNF-treated groups. The levels of retinal glutathione, superoxide dismutase and catalase were significantly increased in BDNF-treated group than in Aβ1-40-treated rats. In object recognition tests, BDNF improved rats' ability to recognise visual cues after Aβ1-40 exposure. Treatment with BDNF abolished Aβ1-40-induced increase in the expression of caspase-3 at the gene

and protein levels in the retina and upregulated TrkB and ERK1/2 expression. In conclusion, our data revealed that co-treatment with BDNF prevents RGC apoptosis induced by Aβ1-40.

Keywords: Amyloid beta 1-40 peptide (Aβ1-40), Retinal toxicity, Flouro-Gold (FG), Brain-derived neurotrophic factor (BDNF), Neuroprotection, Tropomyosin receptor kinase B (TrkB)

OND-02

Protective effects of magnesium acetyltaurate against NMDA-induced retinal damage and visual impairment in rats involves suppression of NF-κB, p53 and AP-1 (c-Jun/c-Fos)

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Progressive loss of retinal ganglion cells (RGCs) resulting in visual field deficits is the hallmark of glaucoma. Magnesium acetyltaurate (MgAT) has been shown to have a protective effect against N-methyl-D-aspartate (NMDA)-induced retinal cell apoptosis. The current study investigated the involvement of nuclear factor kappa-B (NF-κB), p53 and AP-1 family members (c-Jun/c-Fos) in neuroprotection by MgAT against NMDA-induced retinal damage. In this study, rats were divided into 3 groups: group 1 and group 2 received intravitreal injection of vehicle and NMDA, respectively, while groups 3 received MgAT as pretreatment to NMDA. Seven days after injections, retinal ganglion cells survival was detected using retrograde labelling with fluorogold and BRN3A immunostaining. Retinal level of target proteins and their gene expression were assessed using western blot analysis and real-time PCR, respectively. Rat visual functions were evaluated using visual object recognition tests. Overall, our data demonstrated that pretreatment with MgAT suppressed NMDA-induced increase in transcriptional activity of NF-κB, p53 and AP-1 family members (c-Jun/c-Fos), as it was shown by both real-time PCR and western blot analysis. Protective effect of MgAT correlated with the number of preserved RGCs as shown by retrograde labelling with fluorogold and BRN3A immunostaining. The evaluation of visual function of rats demonstrated that MgAT improved difficulties of rats to recognise the visual cues after NMDA exposure, suggesting that visual function of rats was relatively preserved by pretreatment with MgAT. In conclusion, pretreatment with MgAT prevents

NMDA induced retinal damage via downregulation of transcriptional activity of NF-κB, p53 and AP-1-mediated c-Jun/c-Fos.

Keywords: AP-1 (c-Jun/c-Fos), Magnesium acetyltaurate, NF-κB, N-methyl-D-aspartate, Object recognition tasks, p53, Retinal excitotoxicity, Retrograde labelling

OND-03

Effect of *trans*-resveratrol on retinal oxidative stress in rats with NMDA-induced retinal excitotoxicity

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Modulation of adenosine A1 receptor (AA1R) is known to counteract N-methyl-D-aspartate NMDA-mediated excitotoxicity in glaucoma. *Trans*-resveratrol (TR) is neuroprotective compound with antioxidant properties and agonistic activity at the A1 adenosine receptor. As such, it could act as a potential neuroprotective agent in excitotoxicity related retinal damage in glaucoma. Hence, this study aimed to investigate the effects of TR on NMDA-induced retinal oxidative stress in rats. The Sprague Dawley rats (200-250 g) were divided into 4 groups; group 1 and 2 received intravitreal injection of phosphate buffer saline (PBS) and NMDA (160 nmol), respectively. Group 3 received intravitreal injection of 4 nmol TR, 24 hours prior to NMDA injection whereas group 4 received intravitreal injection of 4 nmol TR and 8 nmol DPCPX (AA1R antagonist) as pre-treatment. Seven days after post NMDA injection, rats were euthanized and retinae were collected for assessment of reduced glutathione (GSH), superoxide dismutase (SOD), and catalase (CAT) using ELISA. Lower levels of retinal CAT, SOD and GSH were observed in NMDA group compared to PBS group ($p<0.001$). TR preserved retinal oxidative status as it was evidenced by higher levels of retinal CAT ($p<0.001$), SOD ($p<0.001$) and GSH ($p<0.01$) in TR-treated group compared to NMDA group. Addition of DPCPX abolished the antioxidant effects of TR in the NMDA-damaged retinas. In conclusion, TR protected against NMDA-induced retinal oxidative stress in rats, which is likely to involve stimulation of AA1R

Keywords: *trans*-resveratrol, Adenosine A1 receptor (AA1R), Glaucoma, N-methyl-D-aspartate receptors, ELISA

OND-04

Minocycline ameliorates hippocampal neuronal damage and β-amyloid peptide deposition in LPS-induced alzheimer's disease rat model

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Alzheimer's disease (AD) is a neurodegenerative disorder and the most common type of dementia. Minocycline is a tetracycline derivative with anti-inflammatory properties that has a neuroprotective effect. The study aimed to investigate the neuroprotective effects of minocycline in the LPS-induced AD rat's model. Twenty-five male SD rats were divided into: (i) control, (ii) LPS, (iii) LPS-treated with minocycline 25 mg/kg, (iv) LPS-treated with minocycline 50 mg/kg, and (v) LPS-treated with memantine 10 mg/kg. LPS (5 mg/kg) was administered intraperitoneally once on day 5 while minocycline and memantine were administered intraperitoneally once daily for 14 days. After 24 hr last minocycline administration, hippocampi were dissected for cresyl violet and Congo red staining. The LPS injection significantly ($p < 0.05$) induced neuronal damage in hippocampal and β-amyloid peptide deposition in comparison to control, while administration of minocycline dose-dependently significantly ($p < 0.05$) reversed these effects that comparable with memantine effect. Minocycline may be used as an effective preventive-therapeutic drug for AD.

Keywords: Alzheimer's disease, Hippocampus, Lipopolysaccharide, Minocycline

OND-05

Reinnervation of the soleus muscle and extensor digitorum longus (EDL) muscle following sciatic nerve crush injury treated with *Arthrospira platensis*

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Reinnervation is the restoration process of the nerve supply loss to a part of a body. Sciatic nerve injury commonly results in degeneration of the distal axons and muscle denervation that leads to muscle atrophy. *Arthrospira platensis* have a high source of Gamma Linolenic Acid (GLA), phycocyanin and vitamin B complex. The aim of this study is to observe the motor functional recovery in rat model through muscle weight, behavioural analysis and histological analysis. Four major groups were divided from 104 rats; normal group (n=8), negative control group (n=32) (no treatment administered), positive control group (n=32) (Injured rats administered with 500 µg/Kg/day of methylcobalamin) and the experimental group (n=32) (Injured rats administered with 180mg/kg/day of *A. platensis*). The recovery rate of muscle weight of both soleus and EDL was faster in experimental than in negative control group. Behavioural analysis evaluated by rotarod test showed that the rat given 180mg/kg/day of *A. platensis* exhibit faster onset of motor functional recovery compared to negative control group. After 28 days, the thickness of the muscle fibers in the experimental group signifies the reduced muscle atrophy and have denser Schwann Cell around the myelin sheath. As a conclusion, the results indicated *A.* platensis has the potency to enhance the nerve regeneration to help the reinnervation of muscles.

Keywords: Reinnervation, Sciatic Nerve, Gamma Linolenic Acid (GLA), *Arthrospira platensis,* Regeneration

OND-06

Characterization of the reward structural connectivity in female malay adolescents using diffusion magnetic resonance imaging

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Adolescents have been shown to be more reward sensitive compared to other age groups. Previous studies have also shown that the white matter tracts between the frontostriatal reward-related brain regions is associated with reward sensitivity. Since the reward network of female Malaysian Malay adolescents is understudied, the aim of this study was to characterize the white matter structural connectivity of the frontostriatal reward circuit of 15 healthy female Malaysian Malay adolescents by determining the relative connection probability of nucleus accumbens (NAcc) seed region to six target regions including the amygdala, anterior cingulate cortex (ACC), medial orbitofrontal cortex (mOFC), hippocampus, ventrolateral prefrontal cortex (vlPFC) and dorsolateral prefrontal cortex (dlPFC). This study also investigated the pattern of distribution from the parcellation of the NAcc corresponding to the connectivity of the 6 targets. Diffusion magnetic resonance imaging was used to study the reward structural connectivity via probabilistic tractography which was performed for each subject by calculating the number of streamlines between the seed and each target mask. The result showed that the healthy participants had the highest relative connection probability of NAcc to mOFC, while parcellation showed the widest distribution of connection to mOFC compared to the other 5 targets in both the left and right sides of the brain. In conclusion, this study shows that putative connectivity between

NAcc and mOFC is highest compared to amygdala, ACC, hippocampus, vlPFC and dlPFC. This supports previous study that shows NAcc is highly specific to the connection to mOFC. This finding can be explained by prior evidence showing early maturing of the NAcc-mOFC tract.

Keywords: Reward, Structural Connectivity, White Matter, Adolescent, Diffusion Magnetic Resonance Imaging, Relative Connection Probability, Parcellation

OND-07

Targeting expression of inflammatory markers in cortex and hippocampus of epileptic mice treated with novel drug combination

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Epilepsy is an excitatory neuronal disorder that affects 1% of the world's population. Regardless of the available anti-epileptic drugs, about 35-40% of epileptic patients get resistant to them. This demands the development of new therapies. Recent studies have shown inflammation to play a vital role in the pathophysiology of epilepsy. Therefore, the present study was planned to examine the combined impact of levetiracetam (LEV); a newer antiepileptic drug, and diclofenac sodium (DFS); an anti-inflammatory on epilepsy mice models. NMRI mice were divided into control and treatment groups. LEV alone and in combination with DFS was given for 3 days. On the 3rd day after administering the required drugs pilocarpine challenge was given, intraperitoneally. Behavioral changes were observed for 90 mins after the administration of pilocarpine; for the latency to first seizure, continuous seizures, duration of continuous seizures, and survival rate. After behavioral observations, animals were sacrificed to determine mRNA expression levels of IL-6 and IL-1β in the hippocampus and cortex using RT-PCR. The results showed significant improvement in the latencies to first and continuous seizures, duration of continuous seizure, and survival rate in the combination treatment group. The results showed significant improvement in the latencies to first ($p < 0.001$), continuous seizures ($p < 0.05$), duration of the continuous seizure ($p = 0.001$), and survival rate ($p < 0.01$) in the combination treatment group as compared to the control or individual drug treatment groups. Furthermore, a decrease in the expression of inflammatory markers; IL-6 and IL-1β was also observed in the combination treatment group when compared to groups that were

given PLC and LEV alone. The result of this study shows that DFS enhances the efficacy of LEV and may be given in combination with LEV for epilepsy treatment after further research and investigations.

Keywords: Epilepsy, Inflammation, Pilocarpine, Levetiracetam, Diclofenac Sodium

OND-08

Effect of caloric vestibular stimulation on behavioural changes in chronic mild stress induced rats

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In the current scenario, stress has become a part of life and a common issue that affects all ages and almost all of us experience it at some point in our lives. Stress implies alteration in the physiological balance and the reaction to stress varies largely between individuals. There are numerous vital complications emerging out of stress for which no specific instinctive treatment is identified. Hence, there is an obligation of palliative approaches like vestibular stimulation which can decrease stress and increase mental well-being. Therefore, the current study aimed to evaluate the effect of Caloric Vestibular Stimulation (CVS) on behavioural changes in Chronic Mild Stress (CMS) induced rats. Twenty-four healthy male Sprague Dawley rats divided into four groups (n=6) were used for the study. CMS was induced using various stressors for 28 days. From Day 14 of CMS, bilateral CVS was given with hot water (temperature 400C) for 15 days. Changes in behaviour were measured on day 1, 15 and 28 and the results were subjected to statistical analysis. The CMS-induced group showed significant decrease in locomotor activity, wire grip strength, fall on time and immobilization time on both day 15 and day 28 when compared with the control group. The CMS induced group which received CVS showed significant increase in fall on time, grip strength and immobilization time on day 28 when compared with the CMS group. In conclusion, caloric vestibular stimulation was effective in alleviating the behavioural alterations in chronic mild stress induced rats.

Keywords: Caloric vestibular stimulation, Chronic mild stress, Rats

OND-09

Thalamic probabilistic connectivity with cerebral cortex in spastic cerebral palsy

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Motor impairment is the main disabling impact of cerebral palsy (CP). Whether the pathways between the thalamus to motor cortex in spastic cerebral palsy are disrupted remains unclear and the study on its pattern of connectivity is sparse. Hence, this study aims to investigate the probabilistic connectivity between the thalamus and motor areas of cerebral cortex as well as to assess its correlation with Gross Motor Function Measures (GMFM) in cerebral palsy patients. Tractography was performed on diffusion MRI data of ten healthy control and ten CP patients. Connection probability index, which is the indication of white matter integrity, was measured between the thalamus to each motor cortex. Correlation between the thalamo-cortical connectivity with GMFM was performed in CP patients. The thalamus was further parcellated according to its connection with a specific motor cortex. It has been found that the pattern of thalamo-cortical connectivity in cerebral palsy was variable according to the patient's clinical presentation. The findings revealed that there was no correlation between the thalamo-cortical connectivity with GMFM. Thalamic parcellation in control showed that the thalamic cluster with positive connection to primary motor cortex was associated with the lateral group nuclei, which contain the thalamic motor nuclei. A striking feature of thalamic parcellation in CP was the presence of clusters with positive connection to the supplementary motor area. The findings suggest that the CP brain network was unique according to the clinical manifestation.

There was also evidence of neuroplasticity as a compensatory mechanism for the motor deficit in CP.

Keywords: Diffusion MRI, Cerebral palsy, Tractography, Thalamus, Motor cortex

OND-10

Exonic polymorphisms in dopamine receptor type 2 gene and their association with schizophrenia in Pakistani population: A case control study

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Schizophrenia is a chronic mental illness affecting 1% of the worldwide population. Antipsychotics are the mainstay of treatment for schizophrenia, majority of which target dopamine receptor type 2 (DRD2). Exonic polymorphisms in *DRD2* also affect treatment response, therefore, we investigated exon 7 of *DRD2* gene for these polymorphisms to find their association with schizophrenia in Pakistani population. Overall, 100 Schizophrenia patients and 100 controls were recruited. Genomic DNA was isolated, followed by PCR and Sanger sequencing. Nucleotides were aligned using MEGA-X software against the reference sequence. Results showed no difference in genotype or allele frequency for any of identified known polymorphisms (rs6275, rs6277 and rs1801028) between cases and controls (P>0.05). Interestingly a novel mutation at chr11:113412805 (C>A) was also spotted. Significant difference among cases and controls was also found (P=0.001) for this SNP. Frequency of homozygous wild type genotype (CC) was higher in schizophrenia patients (67%) than in control (43%) group. In contrast, heterozygous genotype (CA) was higher in controls than in cases (57%, 33% respectively). While frequency of mutated allele (A) of this novel mutation was higher in controls than cases (28.5%, 16.5% respectively). Our data showed that A allele might have protective effect and that C allele may be associated with schizophrenia, being found in higher frequency in cases (83.5%) than in controls (71.5%). The actual mechanism conferring this protective effect is not clear.

Apparent lack of association of other polymorphism with schizophrenia may be due to ethnic differences. Multicenter replication studies with large sample size are encouraged.

Keywords: Schizophrenia, Dopamine Receptor Type 2, Polymorphisms, Sanger Sequencing, Genotyping

OND-11

Effect of *trans*-resveratrol on glutamate clearance and visual behaviour due to excitotoxic retinal injury in rats

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Glutamate excitotoxicity underlies retinal glaucomatous optic neuropathy, the leading cause of irreversible blindness. Excitotoxicity involves excessive glutamate-mediated neurotransmission resulting in over-accumulation of Ca^{2+} ions in mitochondria, which in turn causes activation of apoptotic pathway. Glutamate clearance by glial cells through glutamate transporters, EAAT1 & EAAT2, plays a crucial role in regulating extracellular glutamate concentration. Previous studies have shown that *trans*-resveratrol (TR) enhances glutamate clearance by increasing glutamate transporters expression in hyperglycaemic rats. We investigated the same effect of TR in rats with glutamate-induced retinal excitotoxicity. Sixty *Sprague-Dawley* rats were divided into five groups that included one untreated and four groups that received bilateral intravitreal treatment. Control rats received PBS, glutamate-treated rats received glutamate, TR post-treated group received TR 24 hours after glutamate and TR pre-treated group received TR 24 hours before glutamate. Rats were sacrificed on day 8 post-treatment. The retinal expression of glutamate transporters and glutamate concentration were determined using ELISA and glutamate assay, respectively. Retinal morphology was determined using H&E staining. It was observed that the glutamate concentration was higher and retinal layers were thinner in glutamate-treated group compared to all other groups. Whereas, TR-treated groups, particularly the pre-treatment group, showed significantly higher expression of EAAT1 & EAAT2, lower glutamate concentration and preserved retinal morphology. In conclusion, TR protects against glutamate-induced changes in retinal morphology by increasing the glutamate transporter expression and enhancing glutamate clearance in rat retinas.

Keywords: Glutamate excitotoxicity, *trans*-resveratrol, Retinal Injury

OND-12

The neuroprotective effect of zinc oxide nanoparticles against paraquat-induced toxicity

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Parkinson's disease (PD) is a neurodegenerative disorder that affects body movement. Exposure to the herbicide paraquat can increase the risk of developing PD. Oxidative stress plays a major role in the pathogenesis of PD. Zinc oxide nanoparticles (ZnO-NPs) possess antioxidant properties and have been implicated in the treatment of oxidative stress-related diseases. It is hypothesized that ZnO-NPs can be used to treat PD. This study aims to examine the protective effect of ZnO-NPs against PQ-induced cell death in SH-SY5Y cells. The cells were exposed to the following treatment conditions: (i) pre-treated with ZnO-NPs for 24 h, followed by co-incubation with ZnO-NPs and PQ for 48 h, (ii) co-treated with ZnO-NPs and PQ for 48 h, and (iii) pre-treated with PQ for 2 h, followed by co-incubation with ZnO-NPs and PQ for 48 h. The concentration(s) used in this study was 300 μM for PQ and 0.1–1.0 μg/mL for ZnO NPs. Cell viability was evaluated by using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. The 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay was performed to determine the free-radical scavenging activity of ZnO-NPs. We found that the cell viability for the PQ group treated with ZnO-NPs (0.5 μg/mL) was significantly higher ($p < 0.05$) by ~13–18% compared to the group treated with PQ alone for all three treatment conditions. However, ZnO-NPs did not display any direct free radical scavenging activity. In conclusion, ZnO-NPs are neuroprotective as they can attenuate PQ-induced cell death. This study warrants further investigation to determine the neuroprotective mechanisms of ZnO-NPs.

Keywords: Antioxidants, Cell death, Free radicals, Nanoparticles, Oxidative stress, Paraquat, Parkinson's disease, Zinc oxide

OND-13

Treatment satisfaction and medication adherence among patients with epilepsy at daoud charity clinic

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Poor adherence to medication is common especially in the case of chronic diseases like Epilepsy. Treatment satisfaction may impact adherence. The study aimed to measure medication adherence and its relationship to treatment satisfaction, duration of illness and Epilepsy control and to determine the causes of nonadherence in Sudanese patients with epilepsy. This cross-sectional study was conducted in Daoud Charity Clinic. A total coverage of patients with epilepsy fulfilling the inclusion criteria during a period of eight weeks was performed. Patients were interviewed and assessed using Hill-Bone medication adherence scale (HB-MAS) and treatment satisfaction questionnaire for medication (TSQM) to measure medication adherence and treatment satisfaction. 72 patients were studied. 43% were male and 57% were female. Mean age was 31.28 $\pm$ 11.46 years. Mean HB-MAS score was 34 $\pm$ 2.1 indicating high adherence. Adherence was not significantly correlated with duration of illness and there was no significant difference in mean HB-MAS score between patients with well- and poorly-controlled epilepsy. 57% reported to have missed their medication more than once because of short supply. Mean treatment satisfaction scores regarding four domains of effectiveness, side effects, convenience and global satisfaction were 84.5 $\pm$ 17.7, 92.4 $\pm$ 17.1, 83.9 $\pm$ 12.8 and 83.4 $\pm$ 18.8 respectively. There was a significant correlation between adherence and the convenience domain ($p=0.002$), but not the other domains. In our sample medication adherence

and treatment satisfaction was found to be high in patients with epilepsy. Treatment satisfaction in regard to convenience was significantly correlated to medication adherence.

Keywords: Treatment Satisfaction, Medication Adherence, Epilepsy

OND-14

Therapeutic potential of cerium oxide nanoparticles in alzheimer's disease

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Alzheimer's disease (AD) is a crippling illness that is attributed to the aggregation of amyloid beta (Aβ) protein in the brain. Excessive accumulation of Aβ aggregates can promote oxidative stress, resulting in brain cell death. To counteract oxidative stress and free radical production, antioxidant therapy has been implicated in the treatment of AD. Recently, cerium oxide nanoparticles (CONPs) are being explored as a prospective medication to treat AD due to their unique antioxidant capabilities. This systematic review aims to investigate the therapeutic actions of CONPs in AD models to affirm their potential as a medicinal element in treating AD. Keywords that are related to CONPs and AD were used to obtain relevant papers from the PubMed, MEDLINE, and Embase databases from inception to November 2020. A total of 150 records were found and after thorough screening, only 17 research articles met the inclusion criteria. The findings revealed that CONPs have the ability to reverse the harmful effects of oxidative stress as depicted by the improvements in spatial working memory, neuronal vitality, and mitochondrial health along with a reduction in oxidative damage, Aβ aggregation, glial cell activation, and neuroinflammation. In spite of that, a few studies have shown that CONPs can cause toxicity at higher doses. In conclusion, CONPs are a potential treatment option for AD patients because of their valuable therapeutic effects. However, more preclinical studies have to be conducted to maximise the antioxidant potential and to curtail the adverse effects of CONPs.

Keywords: Alzheimer's disease, Amyloid beta protein, Antioxidants, Cell death, Cerium oxide, Free radicals, Nanoparticles, Oxidative stress

PND-01

Neuroprotective effect of tualang honey on kainic acid-induced neurodegeneration in the rat lateral septal area: A preliminary finding

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Lateral septum (LS) plays important role in emotional and stress responses via modulation of neuroendocrine activities. Kainic acid (KA) produces excitotoxic effect which can lead to neurodegeneration. The effects of Tualang honey (TH) in the LS of KA-induced neurodegeneration is still unknown. This study aimed to investigate the neuroprotective effect of TH on KA-induced neuronal changes in the rat lateral septum. Male Sprague Dawley rats were randomly divided into four groups [Control, KA, TH+KA, Topiramate (TPM)+KA]. The rat groups were pre-treated orally with distilled water (control and KA groups), TH (1.0 g/kg) and TPM (40 mg/kg) for five times at 12 hours interval. Then were injected subcutaneously with KA (15 mg/kg: KA, TH+KA and TPM+KA) or normal saline (control) 30 minutes after the last oral treatment. The rats were sacrificed at 24 hours or 5 days after the KA administration. Neuronal changes in LS were assessed using haematoxylin and eosin (H&E), cresyl violet and Fluoro-Jade C (FJC) staining. KA-induced significant reduction in the number of viable neurons in the LS were observed at 24 hours ($p=0.0026$) and 5 days ($p=0.011$) when compared to the control. For FJC analysis, no FJC-positive cell was observed in the control. Pre-treatment with TH or TPM significantly reduced the number of FJC-positive cells in 24 hours subgroup

when compared to KA ($p<0.001$). These results suggested that TH has potential neuroprotective effect by attenuating KA-induced excitotoxicity in the lateral septal region of rats.

Keywords: Tualang honey, Kainic acid, Lateral septum, Neurodegeneration, Histology

PND-02

The effects of tualang honey and its silver nanoparticles on hippocampal oxidative injury in kainic acid-induced male rat

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Kainic acid (KA) mediated excitotoxicity was shown to cause oxidative stress in rats brain. Tualang honey (TH) has revealed a neuroprotective effect, but no study has explored on its silver nanoparticles (THSN). This study aimed to investigate the effects of TH and THSN on KA-induced oxidative damage in rats' hippocampus. Male Sprague-Dawley rats (n=48) were randomized into eight groups: (i)control, (ii)THSN 10mg/kg, (iii)THSN 50mg/kg, (iv)KA only, (v)KA+TH, (vi)KA+THSN 10mg/kg, (vii)KA+THSN 50mg/kg and (viii) KA+Topiramate. The respective groups of rats were pretreated orally with either distilled water, THSN (10 or 50 mg/kg body weight), TH (1.0 g/kg body weight), or Topiramate (40 mg/kg body weight), for five times at 12 hours intervals. Saline or KA (15 mg/kg body weight) were injected subcutaneously after the last oral treatment. The rats were sacrificed 24 hours post KA induction and hippocampus was harvested. Malondialdehye (MDA), total nitrate/nitrite (NOx), gluthathione (GSH) and total antioxidant status (TAS) were

measured using commercially available ELISA kits. A significant decrease was showed in MDA levels in KA+TH (6103.87±207.10 pmol/ml), KA+THSN 10mg/kg (4549.44±914.10 pmol/ml) and KA+THSN 50mg/kg (6349.93±1040.86 pmol/ml) groups compared to KA only (12477.83±2897.40 pmol/ml) group. Similar trend of results for NOx level were observed in KA+TH (45.14±19.72 ng/ml), KA+THSN 10mg/kg (36.11±28.10 ng/ml) and KA+THSN 50mg/kg (58.56±32.29 ng/ml) groups compared to KA only (290.91±75.45 ng/ml) group. Meanwhile, the level of GSH was remarkably increased in KA+THSN 10mg/kg (995.09±161.17 µg/ml) and KA+THSN 50mg/kg (953.69±223.46 µg/ml) group compared to KA only (111.17±43.71 µg/ml) group. There was a significant elevated in TAS level in KA+ THSN 10mg/kg (3139.83±780.09 ng/ml) group compared to KA only (453.90±296.68 ng/ml) group. These findings suggest that the pretreatment with TH and THSN might have potential role to ameliorate oxidative stress in the hippocampus of KA-induced rats. However, further study needs to be conducted to understand the precise mechanism.

Keywords: Silver nanoparticles, Tualang honey, Kainic acid, Hippocampus, Oxidative stress markers

PND-03

Evaluation of anti-convulsant potential of *Orthosiphon stamineus* (Misai Kucing) using an *in vivo* seizure experimental model

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Currently available anti-seizure drugs (ASD) provide mere symptomatic relief of epilepsy rather than a long-term relief. Moreover, some ASDs display several deleterious cognitive and behavioral consequences which may lead to worsening of the epileptic patients. Hence, there is a pressing need to explore alternative therapies that exhibit anti-convulsive activity with fewer side effects than currently available modern ASDs. *Orthosiphon stamineus* (OS) is a common herb, also known as cat's whiskers or "misai kucing". It is a herbaceous shrub and can be found in tropical climates. Its application has been justified by various studies that delineates the secondary metabolites of the plant exerts anti-inflammatory, gastroprotective and antihypertensive effects. To the best of our knowledge, this is the first study to explore the anti-convulsant potential of *Orthosiphon stamineus* in pentylenetetrazol (PTZ) and maximal electroshock seizure (MES)-induced epilepsy in an experimental Balb/C mice model. Our findings suggest that repeated dosage of OS for seven days (50, 100 and 200 mg/kg) did not significantly improve seizure onset time and hind limb extension duration. The pre-treated mice demonstrated little delay in seizure onset after PTZ seizure induction. As for the MES aspect, pre-treatment with OS did not considerably shorten the duration of hind limb extension. Overall, short seven-days treatment with OS did not significantly improve the seizures in the mice model. However, it is suggested to further evaluate the effects of long-term administration of OS and the molecular mechanisms of its anti-convulsive properties.

Keywords: *Orthosiphon stamineus* (OS), Pentylenetetrazol (PTZ), Maximal electroshock seizure (MES), Seizure, Balb/C mice

PND-4

Effect of pleasure-eating toward saccharin intake on beta-endorphin and dopamine secretion in *in vivo* model

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Pleasure-eating is a non-homeostatic overeating and a negative reinforcement for compensating pleasure deficiency that is activated by dopamine, known for positive motivation towards subjective needs. The goal was to identify the relation between pleasure deficit, high dopamine secretion, and overeating palatable food by focusing on beta-endorphin as pleasure neurotransmitter, dopamine as motivation neurotransmitter, and overconsumption of saccharin as an eating reaction. Sprague Dawley rats (n=20) were treated with saccharin added in the commercial rat pallets. Rats were sacrificed and striatum were isolated. Beta-endorphin and dopamine were measured after treated with liquid saccharin using ELISA test and compared with normal groups. Results showed that lower level of beta-endorphin and dopamine were released in groups without saccharin treatment, compared with the higher level of beta-endorphin and dopamine secreted after saccharin treatment. This suggested that non-homeostatic pleasure-deficiency condition, expressed by the lower secretion level of beta-endorphin, stimulates striatum dopamine secretion that leads to consumption of non-nutritive liquid saccharin to compensate non-homeostatic pleasure deficit.

Keywords: Motivation, Emotional eating, Striatum, Dopamine, Beta-endorphin

PND-05

An automated bruxism patient detection system based on machine learning models using physiological signals

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Lack of sleep generated many harmful diseases such as, sleep disorders, psychological problems, and heart diseases. The approximately 9 to 31 % of the current populations in the world are suffering from bruxism. Bruxism is one type of sleep or dental disorder in which individual's grinds and clenches the teeth during unconscious sleep. The aim of this study is to develop an automatic detection system based on machine learning using physiological signals. In this work, we used four channels including EMG1-EMG2, ECG1-ECG2, C4-P4, and C4-A1 and three sleep stages such as w, N1, and rapid eye movement stage with power spectral density approach. In addition, we used decision tree classifier and hybrid machine learning classifier in this study to detect the bruxism. The obtained results shows that the accuracy of the EMG1-EMG2, ECG1-ECG2, C4-P4, C4-A1, combine EMG1-EMG2 with ECG1-ECG2, and Combine C4-P4 with C4-A1 channels using decision tree classifier were found to be 93%, 93%, 81%, 74%, 97%, and 81%, respectively. Additionally, the accuracy of the EMG1-EMG2, ECG1-ECG2, C4-P4, and C4-A1 channels using hybrid machine learning classifier were found to be 98%, 96%, 97%, and 94%, respectively. We concluded that EMG1-EMG2 channels using hybrid machine learning classifier have maximum accuracy (98%). As per our knowledge, this classifier achieved the highest accuracy as compared to

the previously articles. This study can be applied for the mental and cardiac diseases detection system.

Keywords: Bruxism, Dental disorder; DT classifier, ECG, EMG, EEG, Power spectral density, Sleep disorder

PND-06

Effects of prenatal bisphenol a exposure on the NMDA receptor subunits: Association with learning and memory impairment in foetus and adolescent male rat hippocampus

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Learning and memory are cognitive functions depending on the plasticity of synapse in brain development. Environmental perturbations such as prenatal Bisphenol A (BPA) exposure has been shown to influence the development of the brain and behaviours when reaching adulthood. This study was conducted to investigate the effect of prenatal BPA exposure on the N-Methyl-D-Aspartate (NMDA) receptor subunits (GluN2A and GluN2B) in feotus and adolescent male rat hippocampus and its neurobehavioural outcomes. Pregnant Sprague Dawley rats were orally exposed at 5 mg/kg/day of BPA with 0.5% Tween 80 in reverse osmosis water from gestational day 2 until 21 or until spontaneous delivery. The control group were exposed to the same treatment except without BPA. The male litters were raised until postnatal day 35 (PND35). At PND35, the learning and memory ability of the rats were evaluated by open field and Morris water maze tests followed by quantification of GluN2A and GluN2B using ELISA. The finding showed the prenatal BPA exposure significantly reduced the expression of GluN2A ($p<0.05$; $p<0.01$) and GluN2B ($p<0.001$; $p<0.001$) in the feotus and adolescent rat hippocampus. Remarkably, the BPA-treated rats also showed anxiety-related behaviour and impairment in spatial memory compared to

the control group. In conclusion, the reduction of NMDA receptor subunits in prenatal BPA exposure is believed to persist when reaching adolescence hence affecting its learning and memory ability.

Keywords: Bisphenol A; Foetus; Adolescent; NMDA receptor subunits; Learning and Memory

PND-10

Neuroprotective effect of *Labisia pumila* against aluminium chloride-induced alzheimer's disease in rats: A cognitive, behavioral and histological study

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Various mechanisms contribute to Alzheimer's disease such as chronic oxidative stress, and mitochondrial disruption. Aluminium mimics the effect of Alzheimer's disease by promoting reactive oxygen species (ROS). *Labisia pumila* can be used as an anti-oxidative agent because they are defensive towards ROS. This study evaluates the neuroprotective effects of *Labisia pumila* against Aluminium Chloride (AlCl3)-induced Alzheimer's disease in Sprague-Dawley rats. Thirty healthy Sprague-Dawley rats were separated into five groups. Group I was negative control group. The Alzheimer Disease rats is induced by ALCl3 (100mg/kg/day) for 42 days which served as the positive control group in Group II. Two doses of *Labisia pumila* extract (200mg/kg/day and 400mg/kg/day) and Rivastigmine (0.3mg/kg/day) will be co-administered in Group III, IV and V specifically. Morris water maze and elevated Plus maze test were done to access the memory and learning. The brain specimens were processed for histological study by using an inverted microscope. Chronic administration of AlCl3 in Group II for 42 days resulted in progressive deterioration of learning ability and reference memory compared to control group ($p<0.05$). Also, Group II displayed the characteristics of neurodegeneration and amyloid accumulation, as Group III, IV, and V attenuated behavioral deficits and improved memory well as reduced live cells densities. Group III, IV, and V resisted histological changes and exhibited a better morphological

appearance compared to Group II. Our results reflect the neuroprotective effects of Labisia *pumila* against AlCl3-induced Alzheimer's disease in rats.

Keywords: Alzheimer's disease, *Labisia pumila*, Neurodegeneration

PND-11

Transcriptional profiling of alpha-2 Giardin in response to drug treatment in *Giardia intestinalis*

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Giardiasis, which is caused by the intestinal protozoan parasite *Giardia intestinalis*, affects approximately 280 million people around the world. Giardiasis mainly affects school children from the lower socio-economic background, particularly those living in the rural parts of Malaysia. The prevalence of giardiasis in Malaysia has been reported to range from 1.4% to 11.1%. Oral ingestion of as few as ten cysts of *G. intestinalis* can cause infection in human which lead to complications such as severe diarrhea, dehydration and weight loss. There are several antigiardial drugs available for giardiasis treatment; however, issues such as drug resistance, reinfection and recurrence of symptoms have been highly reported. Thus, the finding for a novel potential drug targets is important to control the disease. In this study, we sought to examine the role of alpha-2 giardin in response to drug treatment in *G. intestinalis*. Our results showed that *G. intestinalis* were more susceptible to the action of Mebendazole (MBZ) with IC50 value of 0.06 μM when compared with Metronidazole (MTZ) of 9.177 μM. Trophozoites treated with high concentration of MBZ or MTZ showed significant reduction in viability. The release of reactive oxygen species was not detected in either MBZ or MTZ-treated *G. intestinalis*. We also found that *G. intestinalis* treated with 100 μM MBZ or MTZ showed significant up-regulated expression of alpha-2 giardin ($p \leq 0.05$). In conclusion, these observations suggest that alpha-2 giardin could serve as a potential promising target for future drug design and vaccine development.

Keywords: Giardiasis, Giardia intestinalis, Alpha-2 giardin

PND-12

Factors predicting emotional distress among frontliners during COVID-19 pandemic

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The coronavirus disease 2019 (COVID-19) originating from China has been declared as the most recent worldwide pandemic, in view of the rising mortality and morbidity rates around the globe. The virus has expeditiously spread across borders, affecting people in various parts of the world. COVID-19 exposure puts frontliners at a considerably higher risk of physical and mental consequences as a result of providing care to COVID-19 patients. Specifically, the prevalence of emotional distress among frontliners is increasing. Nevertheless, there is a paucity of study in Malaysia on the factors that predict this matter. Therefore, the goal of this study was to investigate factors associated with depression, anxiety and stress among frontliners during the pandemic of COVID-19. This cross-sectional study enlisted the participation of 402 healthcare workers from the hospitals around Klang Valley. DASS-21 questionnaire was used to assess the emotional distress among the respondents. Data on socio-demographics as well as self-reported body weight and height were collected. The prevalence of self-perceived anxiety, depression, and stress among frontline healthcare workers were 36.3%, 28.6%, and 12.9%, respectively. There was an association between marital status and all domains of emotional distress ($p<0.05$). Gender, medical history, marital status, healthcare position, and body mass index (BMI) category were all found to be significant predictors towards anxiety and depression ($p<0.05$). Further research is recommended to widely explore the outcome of this

study and emphasize the emotional distress issues of frontliners during this COVID-19 pandemic.

Keywords: COVID-19, Frontline healthcare workers, Emotional distress, DASS-21, Anxiety, Depression

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