

ABSTRACT BOOK



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30th SCIENTIFIC MEETING OF MALAYSIAN PHARMACOLOGY AND PHYSIOLOGY

(MSPP), 2016

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YIA001

The Influence of CYP3A4 and CYP3A5 Genetic Polymorphisms on Anastrozole's Pharmacokinetics and Pharmacodynamics in Postmenopausal Breast Cancer patients

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Anastrozole (predominantly metabolized by CYP3A4 and CYP3A5) is one of the first line drugs of choice in the treatment of breast cancer. However, despite its superiority to tamoxifen, a significant proportion of patients either experience breast cancer recurrence or develop severe adverse effects following its use. The objective of this study was to determine the impact of CYP3A4 and CYP3A5 genetic polymorphisms on anastrozole's pharmacokinetics and pharmacodynamics among breast cancer patients. A total of 94 postmenopausal breast cancer women were recruited for this study. Genotyping of CYP3A4*18A and CYP3A5*3 was performed using the conventional polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) while a novel multiplex PCR-RFLP method was used for CYP3A4*4, CYP3A4*18B and CYP3A4*22. Serum anastrozole concentration was determined by a newly developed rapid resolution liquid chromatography (RRLC) method following solid-phase extraction. Our study is the first to report on the frequency of CYP3A4*18B G>A among Malaysians which was found to be high (0.48). CYP3A4*18A T>C occurred at a low (0.03) frequency but CYP3A5*3 A>G was high (0.64). No variant alleles of CYP3A4*4 and CYP3A4*22 were detected. Patients homozygous for CYP3A4*18B G>A and CYP3A5*3 A>G had lower and higher serum anastrozole levels (C_{min}), AUC_{0-t} and AUC_{0-∞} respectively compared to those having the wild types or heterozygous variants. However, no significant difference was observed in anastrozole's t_{1/2} among all the different genotypes of CYP3A4*18B G>A and CYP3A5*3 A>G. Furthermore, no significant difference was observed in anastrozole's C_{min}, t_{1/2}, AUC_{0-t} and AUC_{0-∞} between wild type and variant carriers of CYP3A4*18A T>C. Similarly, no significant association was observed between CYP3A4/CYP3A5 genetic polymorphisms and anastrozole's pharmacodynamics. Our findings indicate that CYP3A4*18B G>A and CYP3A5*3 A>G alleles may be important in the individualization of treatment of breast cancer using anastrozole in future.

Keywords: CYP3A4, CYP3A5, genetic polymorphisms, breast cancer, anastrozole

YIA002

Understanding of Neurochemical Circuit Regulating Fear

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Fear arises in stressful situations that are subjectively perceived as threatening, which is a conserved innate emotion expressed in vertebrates. Exposure of humans to an intensely fearful experience can lead to the development of psychological traumatic disorders, which can be triggered by a variety of stimuli including smell. However, the neuronal circuitry involved in odorant-evoked fear response is not well understood. Habenula, an evolutionary conserved brain region, has been recently considered as a brain region involved in emotional responses and its dysfunction is associated with several neuropsychiatric disorders. We have previously shown a predominant expression of neuropeptide kisspeptin and its receptor (GPR54) in the habenula of zebrafish. We found that administration of kisspeptin significantly decreased the odorant (alarm substance, AS)-evoked fear response. Furthermore, inactivation of habenular kisspeptin neural pathway diminished AS-evoked fear response, suggesting the neuromodulatory role of habenular kisspeptin neurons in odorant-evoked fear pathway. Secondly, we found that kisspeptin administration upregulates serotonin-related genes in the brain. The effect of kisspeptin on AS-evoked fear response was successfully blocked by pretreatment with serotonin receptor antagonists, suggesting the involvement of the serotonergic system in modulation of AS-evoked fear response. Morphological approaches revealed that majority of kisspeptin neurons are glutamatergic and kisspeptin fibers are closely associated with glutamatergic and GABAergic cells, but a very few association with serotonergic neurons. These findings suggest that habenular kisspeptin neurons indirectly act on serotonergic system via interneurons. Taken together, our results showed that habenular kisspeptin neurons play a crucial role in odorant-evoked fear response in zebrafish. As kisspeptin receptor is also present in the habenula of mammals, the role of kisspeptin signaling in odor-dependent fear response could be evolutionarily conserved in vertebrates. Understanding neurochemical basis of olfactory related fear circuitry may lead to develop a new therapeutic strategy for psychological traumatic disorders in future.

Keywords: brain; habenula; odorant; zebrafish; neuropeptide

YIA003

Discovery of Endothelial Barrier Protection by Natural Product

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Vascular endothelial cells emerge as a key regulator of vascular homeostasis. Disruption of vascular endothelial barrier leads to vascular hyperpermeability which in turn contributes to a broad spectrum of the most dreadful of human diseases, including heart diseases, diabetes, atherosclerosis, and cancer. The search for permeability-modulating agent still far lacking, thus, it is a need to search for a new agent to reduce endothelial hyperpermeability. *Bixa orellana* L. has been traditionally used to treat a number of ailments, including internal inflammation. Preliminary data showed that its leaves are able to suppress inflammation induced by carrageenan. Hence, this study aimed to investigate the anti-hyperpermeability effect of *B. orellana* leaf extract (AEBO) and elucidate its mechanism of action induced by histamine. The anti-hyperpermeability activity of the extract was evaluated using histamine-induced rat paw oedema, increased peritoneal vascular permeability, nitric oxide (NO) and vascular endothelial growth factor (VEGF) measurement in animal model, while, phospholipase C (PLC) – NO – cyclic guanosine monophosphate (cGMP) signaling pathway was determined via in vitro. AEBO produced a significant inhibition of histamine-induced paw edema starting at 60 min time point, with maximal percentage of inhibition (60.25%) achieved with a dose of 150 mg/kg. Up to 90% of increased peritoneal vascular hyperpermeability successfully suppressed by AEBO. NO and VEGF from inflamed paw tissues was also found to be downregulated in the AEBO group. Histamine-induced increased endothelial permeability was significantly attenuated by pretreatment with AEBO in a time- and concentration-dependent manner. Moreover, AEBO also suppressed PLC, calcium, NO and cGMP signaling cascade when endothelial cells were challenged with histamine. Protein kinase C activity was also significantly abolished by AEBO under histamine condition. In conclusion, the present data suggest that AEBO could suppress histamine-induced increased vascular permeability and the activity may be closely related with the inhibition of the PLC-NO-cGMP signaling and PKC activity.

Keywords: *Bixa Orellana*, histamine, vascular permeability

ORA001

Application of Positron Emission Tomography (Pet) Nuclear Imaging in Novel Anticancer Drug Development

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Positron Emission Tomography (PET) is a powerful nuclear medicine imaging tool that produces high quality three-dimensional images of functional processes of body. In a PET study, positron emitting radiopharmaceuticals which are produced in a cyclotron, are administered into the body. During the decay process, the emitted positrons travel a short distance and undergo annihilation with a nearby electron. The annihilation process produces two gamma photons with the energy of 511KeV each. These high energy gamma rays pass through the body and are detected by coincidence detector of PET. The advantages of the PET among all other imaging devices is that it allows whole-body physiologic imaging study within a single imaging session. Combined PET and CT allows the viewing of both the function and anatomy of the tissue of interest with a single scan. The abilities of PET/CT to study early treatment response and drug distribution within the body makes this technique a powerful tools in the assessment of the effectiveness of new anticancer drugs at an early development stage. This paper will highlight the current role of PET/CT in novel anticancer drug research and development.

Keywords: PET, radiopharmaceuticals, nuclear imaging, drug development

ORA002

Alteration in Salivary Parameters Leads to Oral Lesions among Chewable Tobacco Users

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Salivary glands produce saliva which plays an important role in maintaining oral health of teeth and soft tissues. The health of oral mucosa depends on oral clearance which, under resting conditions, depends on salivary parameters i.e. salivary flow rate and its pH. Chewable tobacco is an integral cultural component of majority of South East Asian countries, is a cause of corrosive consequences on oral mucosa. Salivary flow and its composition alter under deleterious chemical irritants present in chewable tobacco. Apart from inflammation and deterioration in health of oral mucosa it can also affect the major and minor salivary glands and cause a decline in salivary flow rate. This study was designed to find out alteration in salivary parameters that lead to oral lesions among chewable tobacco users. A total of 354 healthy male subjects, consuming any form of chewable tobacco product, belonging to low socioeconomic areas of Karachi, Pakistan were selected for this cross sectional study. Chewable tobacco products widely consumed in Pakistan are gutka, paan and niswar, Tobacco, sun-dried roasted, finely chopped or powdered, is the main ingredient of these products combined with other ingredients such as ash, oil flavoring agents, lime, areca nut and betel leaf varying from product to product. These are either chewed constantly such as gutka and paan or placed and held under the tongue or in buccal mucosa for long periods of time such as niswar. A questionnaire was used to collect demographic data and details of chewing habits (using since, pack/day, duration of exposure etc.). Resting saliva of every subject was collected for 5 min and Resting Salivary Flow Rate (RSFR) was expressed in ml/min. Salivary pH was determined by using pH strips (pH 0-14). Oral examination was done for the presence or absence of oral lesions. Out of the 354 subjects included, 27.4% consumed gutka, 24.3% niswar, 24.3% paan and 24% were multiple users. Mean RSFR was 0.52 ± 0.34 ml/min and pH 6.58 ± 0.78 . Among these 96 (27.1%) had oral lesions with highest frequency observed among subjects who had hypo salivation (40%) and those having acidic pH (40%). There was significant decrease in RSFR and pH and increase in frequency of oral lesions is observed with increased duration of exposure, duration of usage and increased number of tobacco packs consumed per day.

Keywords: Saliva, Tobacco chewing, oral lesions

ORA003

Stimulation of Hair Growth Using Ethanolic Extract of Mixed Chinese Herbal Medicine (CHM)

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Every year, billions of dollars had been spent globally in hope to find a curative treatments for hair loss, but unfortunately many of the treatments are questionable due to their occasional lack of efficacy, safety and their potential side effects. Chinese herbal medicine (CHM) with more readily accessibility and rare side effects has gained more attention recently in treating hair loss problem. The aim of this study was to investigate the efficacy and safety of HAO product, an ethanolic extract of mixed CHM as hair growth promoter. This was a single armed, single blinded study conducted among 16 healthy subjects aged 30 years and above. Treatment given was ethanolic extract of six mixed CHM, which included *Polygonum multiflorum*, *Morus alba*, *Thuja occidentalis*, *Angelica sinensis*, *Ligusticum striatum* and *Chenopodium ambrosioides*. All subjects were required to apply treatment twice daily up to 210 days. The efficacy measure was the changes in the scalp coverage by hair by using Calibrated Scalp Coverage Scoring (CSCS). Demographic data showed almost equal ratio between gender, 1:1.28 respectively for male and female. The mean (SE) number of CSCS among subjects at baseline was 26.81 (4.45), and has been greatly reduced to 20.03 (16.24) after treatment, the difference observed was significant ($P<0.01$). Although no significant association was found with age or scalp type, but it did show a significant association with the duration of usage. The efficacy of treatment was significantly higher ($P<0.05$) after 210 days of usage as compared to other short terms users. Additional improvement after treatment included hair shine and reduced grey hairs. No adverse events were reported. In conclusion, HAO product can effectively and safely promote significant hair growth regardless of gender, and its efficacy increased with duration of usage.

Keywords: Hair Growth, Chinese Herbal Medicine (CHM), HAO Product, Ethanolic Extract

ORA004

Efficacy of *Cordyceps Sinensis* as an Adjunctive Treatment in Continuous Peritoneal Dialysis Patients: A Systematic Review and Meta-analysis

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Despite well-documented benefits of *Cordyceps sinensis* (cordyceps), its efficacy remains controversial in patients undergoing continuous ambulatory peritoneal dialysis (CAPD). This review examines current evidence on the efficacy and safety of cordyceps or its fermented products used as adjuvant in CAPD patients receiving conventional treatment. Methods: We searched Cochrane Central Register of Controlled Trials, EMBASE, MEDLINE, China National Knowledge Infrastructure (CNKI) and Wanfang Data for relevant randomized controlled trials from inception to May 2016. Two review authors independently selected trials for inclusion, extracted data, assessed the methodological quality and rated the quality of evidence with the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach. Seven studies with 397 patients were included. Evidence of low to very low-quality showed that cordyceps versus control did not significantly improve serum C-reactive protein (WMD -2.58 mg/L; 95% CI -5.44 to 0.28), albumin (WMD 2.45 g/L; 95% CI -1.11 to 6.01), hemoglobin (WMD 4.01 g/L; 95% CI -4.62 to 12.64) and serum creatinine (WMD -37.36 μ mol/L; 95% CI -83.90 to 9.18). Similarly, there were no statistically significant differences between the two groups in the reduction of peritonitis (RR 0.39; 95% CI 0.14 to 1.12) and exit-site infection (RR 0.39; 95% 0.08 to 1.86). Adverse events were not reported in most of the included studies. Given the methodological flaws and the very low quality of the evidence, current evidence does not support the adjunctive use of cordyceps in CAPD patients.

Keywords: *Cordyceps sinensis*; adjuvant; end-stage renal disease; peritoneal dialysis; meta-analysis

ORA005

A Study on the Knowledge, Attitude and Practice of Reporting Adverse Drug Reactions among Health Care Professionals in a Tertiary Care Teaching Hospital

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Adverse Drug Reactions (ADRs) are an important cause of morbidity and mortality worldwide. Spontaneous reporting of ADRs has played a major role in the detection of suspected, serious, and unusual ADRs previously undetected during the clinical trial phases. Proper monitoring for the prevention and the management of ADRs is need of the hour. The objective of the study was to assess the knowledge, attitude and practice of ADR reporting among health care professionals in a tertiary care teaching hospital. Health care professionals comprising of interns and clinical post-graduates were included in the study (n=152). Participation in the study was voluntary and without any obligation. The study was rolled out after receiving the approval from the Institutional Ethics Committee. The prevalidated questionnaire consisting of a total of 24 items was distributed to the health care professionals. The data was analysed using Chi square test, one way ANOVA and Karl Pearson's co-efficient tests with the help of SPSS software 20.0. Out of 152 participants, 48(31.58%) were year 1, 44(28.95%) were year 2 clinical post-graduate students; as compared to 60(39.47%) interns. Thirty two (21.1%) participants out of which 20 interns, 7(14.6%) year 1 and 5(11.4%) year 2 clinical postgraduates, had knowledge of the local peripheral monitoring centre. The difference was found to be statistically significant ($p < 0.05$). 88.2% of the total participants had never reported an ADR to the pharmacovigilance centre. There was no significant difference among the three groups of the participants, in terms of mean scores of knowledge, attitude and practice ($p > 0.05$), but there was a significant ($p < 0.05$) and positive co-relation between knowledge and practice ($r = 0.2110$) and attitude and practice ($r = 0.2415$). The training of pharmacovigilance activities should start early in the professional training of doctors and needs to be reinforced during the postgraduate course. There is a great need to create awareness regarding Pharmacovigilance and to promote the reporting of ADR amongst health care professionals.

Keywords: pharmacovigilance, health care professionals, questionnaire, under reporting

ORA006

The Knowledge and Practice of Taking Dietary Supplements among General Population of Ipoh.

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Dietary supplements consumption has increased worldwide. The term dietary supplement includes herbs and botanicals as well as vitamins, and minerals and other nutritional supplements. The vitamin supplement market itself is one of the world's fastest growing industries. Most of the general population now is more health conscious. The long-term potentially dangerous effects related to an indiscriminate consumption of dietary supplements are still unknown and are becoming a matter of public health concern. Objective of the study was to determine the knowledge and practice of intake of dietary supplements among the general population in Greentown, Ipoh. It was a cross-sectional study among the general population in Greentown, Ipoh. A questionnaire was used to identify the respondents' social-demographic background, to assess the level of knowledge regarding dietary supplements, and their intake of any supplements for the past 6 months. They were also asked for the reasons behind their intake in the questionnaire. The study assessed the sources on which the respondents acquired their knowledge on supplements. The data collected was analysed using SPSS 17 program. The knowledge level of dietary supplements among the respondents were classified on scores as good (9-12), moderate (5-8) and poor (0-4). Comparison was made with knowledge and dietary intake of supplements. A total of 150 respondents, males 55(36.7%) and females 95 (63.3%) completed the questionnaire survey. 81(54%) had a good knowledge and 89 (60%) had taken supplements for the past six months. Significant correlation ($p < 0.001$) was found with the knowledge and intake of supplements. Present study provide insight into the consumption of dietary supplements. Commercial drive of the pharmaceutical companies to be assessed for the excessive sale through the media. We need to foster the awareness about the correct use of supplements among the population.

Keywords: Dietary supplements

ORA007

Standardized Ethanolic-water Extract of *Ficus Deltoidea Angustifolia* Decreases Blood Pressure in Spontaneously Hypertensive Rats

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Despite the availability of a wide range of drugs, hypertension still remains poorly controlled in many instances. There is still a need to develop better antihypertensive medications. In this regard, medicinal tropical plants could provide alternatives for the treatment of hypertension. This study therefore, examines the antihypertensive effect of a standardized ethanolic-water extract of *Ficus deltoidea Angustifolia* (FD-A) in spontaneously hypertensive rats (SHR). Methodology: Eighteen male SHR, aged 12-14 weeks with blood pressure above 150/90 mmHg were given via oral gavage either 0.5 ml distilled water (control) or 800 mg/kg FD-A or 10 mg/kg losartan daily for 4 weeks. Blood pressure was measured every week using tail-cuff plethysmography. Bodyweight, blood pressure and urine protein were measured on weeks 0 and 4. Data were analyzed using two way ANOVA. Bodyweight increased over the 4 weeks in all the groups. However bodyweight was not significantly different between the 3 groups. Systolic and diastolic blood pressures in rats given FD-A and losartan at week 4 were significantly lower than those in the control group ($p < 0.01$). Urinary protein excretion at week 4 was significantly lower in FD-A and losartan treated rats ($p < 0.001$). Ethanolic-water extract of *Ficus deltoidea Angustifolia* when given at 800 mg/kg daily decreases blood pressure and protein excretion in spontaneously hypertensive rats.

Keywords: *Ficus deltoidea Angustifolia*, Hypertension, Spontaneously Hypertensive Rats.

ORA008

***Labisia Pumila* Water Fraction Reduces Vasoconstriction of Spontaneously Hypertensive Rats Aortic Ring Preparation**

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Labisia pumila, locally called Kacip Fatimah, has been reported to have a wide range of activities including estrogenic, anti-oxidant, anti-aging and anti-cancer but there is no report so far on its vascular activities. Since our preliminary study showed that water extract of *Labisia pumila* caused vasorelaxation on isolated spontaneously hypertensive rat (SHR) aortic ring preparation, thus, the current study aims to fractionate the extract to three fractions and elucidate the possible mechanism(s) of relaxation of the most active fraction. Water extract of *Labisia pumila* was subjected to liquid-liquid extraction using ethyl acetate and followed by n-butanol to obtain 3 fractions; EAF-LPWE (ethyl acetate fraction), BF-LPWE (n-butanol fraction) and WF-LPWE (water fraction). The WF-LPWE was found to be the most potent in relaxing SHR aorta which has been pre-contracted with phenylephrine (PE). The vasorelaxation mechanism of action of WF-LPWE was studied in isolated SHR aortic ring preparation. The cumulative dose response curve of PE-induced (10^{-10} - 10^{-3} M) and KCl-induced (10 - 90 mM) contraction was examined in the presence of WF-LPWE 0.5, 1.0 and 2.0 mg/ml. Subsequently the vasorelaxation effect of WF-LPWE was assessed on aortic rings pre-contracted with PE (1 μ M). The vasorelaxation effect induced by cumulative doses of WF-LPWE (0.01 μ g/ml - 3.0 mg/ml) without and in the presence of nitric oxide synthase inhibitor (N ω -nitro-L-arginine methyl ester (L-NAME); 10 μ M), cyclic-GMP inhibitor, methylene blue (10 μ M), prostaglandin synthesis inhibitor, indomethacine (10 μ M) and cholinergic blocker, atropine (1 μ M) were examined. WF-LPWE (0.5, 1.0 and 2.0 mg/ml) non-competitively inhibited ($P < 0.001$) the dose-response curve of PE and KCl. However, L-NAME, methylene blue, indomethacine and atropine did not significantly alter the vasorelaxation effect of WF-LPWE. It suggests that WF-LPWE exerts vasorelaxation effect not through inhibition of receptor-operated calcium channels, voltage-gated calcium channels nor involving endothelium but possibly by inhibiting the release of calcium from intracellular calcium store.

Keywords: *Labisia Pumila*, vasoconstriction, hypertensive

ORA009

Resibufogenin Prevents Leptin-induced Increases in Blood Pressure during Pregnancy in Sprague-dawley Rats

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Abstract:

Exogenous leptin administration has been shown to significantly increase systolic blood pressure and urinary protein excretion during pregnancy in the rat. Marinobufagenin (MBG) has been implicated in hypertension and proteinuria of pregnancy. The link between leptin-induced rise in blood pressure and marinobufagenin is unknown. It is also unknown if resibufogenin, an MBG antagonist, prevents leptin-induced increase in blood pressure. This study therefore investigated the effect of resibufogenin on leptin-induced raised blood pressure during pregnancy in the rat. Forty-eight female Sprague-Dawley rats, aged 12 weeks, were randomized into 4 groups. Group 1 was given normal saline (Control). Group 2 was given 120µg/kg/day of leptin (LEP), Group 3 was given 120µg/kg/day of leptin +30µg/kg/day of resibufogenin (L+RBG) and Group 4 was given 30µg/kg/day of resibufogenin (RBG) daily from day 1 of pregnancy. Systolic blood pressure, body weight and 24-h urine protein excretion were measured at days 0 and 20 of pregnancy. Animals were euthanized on day 21 of pregnancy for estimation of fetal number, fetal weight and placenta weight. Compared to the control group, systolic blood pressure and urine protein excretion were significantly higher ($p<0.05$), whereas fetal weight was significantly lower ($p<0.05$) in the LEP group. No significant differences were evident in systolic blood pressure, urine protein excretion and fetal weight between control and L+RBG groups. No significant differences were evident in maternal body weight, placenta weight and fetal number between the four groups. Resibufogenin prevents leptin-induced increases in systolic blood pressure, urinary protein excretion and decreases in fetal weight. It appears that MBG might have a role in leptin-induced increase in blood pressure and proteinuria during pregnancy in the rat.

Keywords: Leptin, resibufogenin, hypertension

ORA010

Lipid Modulation Activity of *Garcinia Atroviridis* Extract on 3T3-L1 Cell Line

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Obesity is a global public health problem and it is a risk factor for many chronic diseases such as diabetes mellitus, cardiovascular illness and cancer. Malaysia has been rated as the highest among Asian countries for obesity. The fruit rind of *Garcinia atroviridis*, also known as "Asam Gelugor"TM, is one of sources for hydroxycitric acid (HCA). HCA is a phytochemical that have potential as weight management agent and it recently gained popularity among public. This present study was done to investigate the lipid modulation ability of *G. atroviridis* fruit extract in vitro using 3T3-L1 cell line. Fresh fruit of *G. atroviridis* was macerated using ethanol, rota-vapourised and freeze-dried yielding powdered extract. Then, cell viability assay was conducted using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide salt (MTT). Three concentrations were chosen to be used in adipocyte differentiation, adipolysis and leptin assay. Differentiated adipocytes were analysed qualitatively and quantitatively using Oil Red O stain. Adipolysis and leptin assay was done using adipolysis and leptin ELISA kits respectively. Fruit extract was found to be not toxic on cell line used. At 10, 45 and 60 µg/mL concentrations tested, the extract inhibit adipocytes differentiation significantly as compared to HCA salt. Leptin released was also decreased at increasing concentration used. Meanwhile, the same concentrations tested was found to be promoting adipocyte breakdown as measured by glycerol concentration. Based on our present findings, the *G. atroviridis* fruit can be proposed as one of weight management agents due to its lipid modulation properties.

Keywords: 3T3-L1, *Garcinia atroviridis*, adipogenesis, adipolysis, leptin

ORA011

Effects of Imidazobenzimidazoles Based Compounds on Intraocular Pressure of Ocular Normotensive Rats.

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Intraocular pressure (IOP) is an essential pressure inside the eye that help to maintain the eyes shape and structure. Healthy IOP are maintained by the balance between the continuously produce aqueous humor and its drainage system and by disrupting this balance, it can cause an elevated IOP which significantly increase the risk of glaucoma. Glaucoma is the 2nd leading cause of irreversible blindness worldwide and managing IOP are still the main treatment in glaucomatous eye. Over the last few decades, several numbers of pharmacotherapies shown to be effective in lowering an elevated IOP, however these therapies are come with adverse side effects. To discover novel IOP lowering agents, a total of 28 imidazobenzimidazoles based compounds were screened. This study was done in normotensive rats and rebound tonometry was used to estimate IOP. Compounds were prepared in 3 different concentrations (0.1%, 0.2% and 0.4%) and single dose of this compound were topically instilled onto one of the eye and the other eye were taken as control. Pattern of changes in IOP were observed in 6 time points (0, 0.5, 1, 1.5, 2, 3, 4, 5, 6) include baseline. The compounds IOP lowering activity were determine by assessing IOP maximum decrease from baseline and control, duration of activities and area under curve (AUC). RU 477, RU 552, RU 555, and RU 615 shown at least 25% IOP reduction from both baseline and control, with 5 hour activities and at least 15 AUC. All others compounds shown none, weak and inconsistency in lowering IOP. We concluded that RU 552, RU 555, RU 612, and RU 839 exhibit a significant IOP lowering effect in normotensive rats.

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Keywords: Drug Screening, Glaucoma, Intraocular pressure, Imidazobenzimidazoles,

ORA012

***Lactobacillus Casei* Strain C1 Mitigates Vascular Changes in Spontaneously Hypertensive Rats**

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Hypertension can be caused by various factors while the predominant causes include increase in body fluid volume and resistance in the circulatory system that elevate the blood pressure. Consumption of probiotics has been proven to attenuate hypertension; however, the effect is much strain-dependent. In this study, a newly isolated *Lactobacillus casei* (Lb. casei) strain C1 was investigated for its antihypertensive properties in spontaneously hypertensive rats (SHR). Lactic acid bacteria (LAB) suspension of 11 log colony-forming unit (CFU) was given to SHR (SHR+LAB, n=8), and phosphate buffer saline (PBS) was given as a control in SHR (SHR, n=8) and in Wistar rats as sham (WIS, n=8). The treatment was given via oral gavage for 8 weeks. The results showed that the weekly systolic blood pressure (SBP), mean arterial pressure (MAP), diastolic blood pressure (DBP) and aortic reactivity function were remarkably improved after 8 weeks of bacterial administration in SHR+LAB. These effects were mostly attributed by restoration of wall tension and tensile stress following the bacterial treatment. Although not statistically significant, the level of malondialdehyde (MDA) in SHR+LAB serum was found declining. Increased levels of glutathione (GSH) and nitric oxide (NO) in SHR+LAB serum suggested that the bacterium exerted vascular protection through antioxidative functions and relatively high NO level that induced vasodilation. Collectively, Lb. casei strain C1 is a promising alternative for hypertension improvement.

Keywords: Antioxidant; Blood pressure; Nitric oxide; Probiotic; Vascular reactivity

ORA013

Standardized Aqueous Ethanolic Extract of *Ficus deltoidea Kunstleri* Reduces Blood Pressure in a Dose Dependent Manner in Spontaneously Hypertensive Rats.

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Ficus deltoidea (FD) has a long history of use among the traditional healers and is known for its diverse therapeutic potentials. Studies have shown that the extract of FD has anti-diabetic, wound healing, anti-oxidant and anti-inflammatory effects. It has recently been shown to have an inhibitory effect on angiotensin converting enzyme in vitro. However, its anti-hypertensive effects have not been verified in vivo. This study therefore examined the dose dependent effects of aqueous ethanolic extract of FD on blood pressure in spontaneously hypertensive rats (SHR). Thirty, male SHR aged 12 – 14 weeks, with blood pressure of more than 150/90 mmHg were divided into 5 groups (n=6) that included a control group (group I-received 0.5 ml of distilled water) and three treatment groups (group II-IV). The treatment groups consisted of 500 mg/kg body weight (group II), 800 mg/kg body weight (group III), 1000 mg/kg body weight (group IV) and losartan 10 mg/kg BW (group V). Treatments were given via oral gavage daily for 4 weeks. Blood pressure was measured weekly using tail cuff plethysmography (CODA). Two way ANOVA was used for statistical analysis and P<0.05 was considered significant. Mean reductions in systolic, diastolic and mean arterial pressure (MAP) of group IV at week 4 were 13.79, 27.26 and 21.73 % respectively. Systolic, diastolic and MAP in group IV were significantly lower than those in the control, group II and group III but were not different from those in group V. Area under curve (AUC) showed significantly greater antihypertensive effect of FD in group IV compared to groups II and III (P=0.000). There was no difference in AUC between groups IV and V. Aqueous ethanolic extract of *Ficus deltoidea Kunstleri* at 1000 mg/kg has a significant anti-hypertensive effect in SHR.

Keywords: *Ficus deltoidea*, SHR, Hypertension

ORA014

Hexane Fraction of *Zingiber Officinale* Rhizome Enhances Relaxation of Aortic Rings in Spontaneously Hypertensive Rats

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Zingiber officinale (*Z. officinale*) commonly known as ginger or Halia (local name) has been traditionally claimed to possess antihypertensive effects. Regulation of vascular resistance vessels have been implicated in hypertension. Thus, this study investigates the effects of *Z. officinale* rhizome on the vascular reactivity of spontaneously hypertensive rats (SHRs). The antihypertensive evaluation using various extracts of *Z. officinale* suggested that petroleum ether extract (ZOP) showed the best pharmacological action. Petroleum ether extract was subjected to liquid-liquid fractionation by separation technique to obtain three fractions; HF-ZOP (hexane fraction), CF-ZOP (chloroform fraction) and WF-ZOP (water fraction). The evaluation using various fraction of ZOP suggested that HF-ZOP is the most potent fraction that exhibit anti-hypertensive effects prior proceed to mechanisms. Vasorelaxation effect of hexane fraction of HF-ZOP was evaluated on male SHRs aortic ring. Isolated thoracic aortic rings (n = 6) were harvested and were subjected to endothelium-dependent relaxation studies, pre-contracted with phenylephrine (PE, 1 μ M) and incubated with different antagonists such as N ω -nitro-L-arginine methyl ester (L-NAME, 100 μ M), indomethacin (10 μ M), methylene blue (10 μ M), atropine (1 μ M), glibenclamide (10Mm) and prazosin (0.01 μ M). Incubation with L-NAME, indomethacin, methylene blue and atropine showed significantly potentiated vasorelaxation effects of HF-ZOP. Furthermore, glibenclamide showed inhibitory effects. Collectively, these findings suggest that hexane fraction of *Z. officinale* possibly exerts vascular relaxation mechanisms in SHRs mediated through endothelial-derived nitric oxide-cGMP relaxant pathway and prostacyclin pathways, involvement of muscarinic receptor and possibly by activation of K⁺ATP channel.

Keywords: *Zingiber officinale*, vascular reactivity, antihypertensive, relaxation, aortic rings

ORA015

Evaluation on Elevated Blood Pressure and Serum Analysis of Spontaneously Hypertensive Rat (Shr) Model Treated with *Azadirachta Excelsa* Leaf Extract

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Hypertension or high blood pressure is commonly related to an exponential increase of the cytosolic enzymes creatine phosphate kinase (CPK) and lactate dehydrogenase (LDH) in serum level. Both are the important biomarkers indicating heart injury resulting from myocardial ischemia in hypertension. The study therefore, aimed to determine the effects of *Azadirachta excelsa* ethanolic leaf extract on elevated blood pressure and serum analysis of CPK and LDH level. Twenty-four males of 14 old weeks SHR were randomly assigned into four different groups where (n=6) as followed; Group I , SHR hypertensive control was received distilled water; Group II, SHR was received 250 mg/kg of *Azadirachta excelsa*; Group III, SHR was received 10 mg/kg of quercetin; and Group IV, SHR was received 40 mg/kg of captopril. Meanwhile, normotensive Wistar-Kyoto (WKY; n=6) rats were received distilled water. The treatment was given in 28 consecutive days where the blood pressure was taken weekly. Initially, systolic blood pressure (SBP) and diastolic blood pressure (DBP) of SHR were significantly high ($P<0.05$) compared to WKY. The treatment with *Azadirachta excelsa* reduced both SBP and DBP ($P<0.05$) comparable to quercetin and captopril treated group. On the other hand, it was found that *Azadirachta excelsa* was also successfully reduced both serum level of CPK and LDH at 46% and 31% of reduction respectively. Thus, current findings strongly suggest that *Azadirachta excelsa* might attenuate hypertension via alleviating excess CPK and LDH in hypertensive rat model.

Keywords: hypertension, serum level, *Azadirachta excelsa*.

ORA016

Antihypertensive Effect of Standardised Aqueous Ethanolic Extract of *Ficus Deltoidea* Trengganuensis in Spontaneously Hypertensive Rats

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Ficus deltoidea is one of medicinal plants that has been claimed to have antihypertensive properties. However, scientific evidence about its antihypertensive activity remains undetermined. This study therefore evaluates the antihypertensive effect of a standardised aqueous ethanolic extract of *Ficus deltoidea* trengganuensis (FDT) in Spontaneously Hypertensive Rats (SHR). Thirty, male SHR, aged 12 to 14 weeks, with blood pressures of more than 150/90 mmHg were divided into 5 groups (n=6). Each group was treated daily via the oral route for 4 weeks either with 800, 1000 or 1200 mg/kg body weight of standardised aqueous ethanolic extract of FDT. Controls were given either 10 mg/kg body weight of Losartan or 0.5 ml of distilled water. Blood pressure was measured weekly using tail cuff plethysmography (CODA). Data were analysed using two-way ANOVA. No statistically significant differences were evident between control and FDT treated groups. Systolic blood pressure however was significantly lower in the Losartan treated group when compared to that in the control and groups given 800 and 1000 mg/kg body weight of FDT. However, systolic blood pressure in the group that was given 1200 mg/kg body weight of FDT was slightly lower than that in the control and the other two FDT treated groups and was not significantly different from that in the group given Losartan. Although no significant differences were seen in systolic blood pressure between control and FDT treated rats, systolic blood pressure in rats given 1200 mg of FDT was nevertheless slightly lower than that in the control group; suggesting that perhaps a higher dose or a longer duration of treatment is required to significantly decrease the blood pressure.

Keywords: *Ficus deltoidea*, Hypertension, SHR

ORA017

Topically Applied Tocotrienol Delays Cataract Progression in Streptozotocin-Induced Diabetic Rats by Restoring Lenticular ATP and ATPases Activities

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To investigate the effects of topical application of tocotrienol, a potent antioxidant, on lenticular ATP, ATPases and calpain2 activity in rats with streptozotocin-induced diabetic cataract. Diabetes was induced in Sprague Dawley rats by single intraperitoneal injection of streptozotocin. The diabetic rats were divided into 2 groups that were treated with vehicle (DV) or tocotrienol (DT). A third group of normal rats received vehicle treatment (N). All treatments were given topically and bilaterally for 8 weeks. During 8 weeks of experimental period, lenticular changes were monitored weekly using a portable slit lamp. Subsequently, rats were euthanized and lenses were subjected to estimation of ATP, ATPases and calpain 2 activities and proteins. Both the diabetic groups, DV and DT, showed the onset of cataract three weeks post-STZ injection. However, from fourth week until the end of experimental period there was delay in the progression of cataract in tocotrienol treated rats as indicated by significantly lower opacity index in DT compared to DV at all time-points ($p < 0.05$). This delay in the progression of cataract in DT was observed despite persistent hyperglycemia. Lenticular ATP was restored to normal in DT and was significantly higher than DV ($p < 0.01$). Similar observations were made for the ATPases activities. Lenticular $\text{Na}^+ \text{K}^+$ ATPase, plasma membrane Ca^{2+} ATPase and sarcoplasmic/endoplasmic reticulum Ca^{2+} ATPase activities in DT were higher by 1.37-, 1.29- and 1.25- folds, respectively, compared to DV. Lens calpain 2 activity was significantly lower and soluble: insoluble protein ratio was significantly higher in DT compared to DV. Topical application of tocotrienol delays the progression of cataract in streptozotocin-induced diabetic rats by normalizing the lens ATP level and $\text{Na}^+ \text{K}^+$ ATPase and Ca^{2+} ATPase activities, which resulted in reduction of calpain 2 activity and preservation of soluble: insoluble protein ratio.

Keywords: Tocotrienol, Oxidative stress, ATP, ATPase, Calpain, Cataract

ORA018

***Erythroxylum Cuneatum* Potentially Attenuates Morphine-dependent In Cell Line**

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Morphine and most of the other opioid drugs are known to be used clinically as analgesia since it has potent analgesic effects. The uses of morphine or opioids cause the development of tolerance, hyperalgesia, dependence, and unpleasant motivational withdrawal. Receptor desensitisation is one of the characteristics of morphine that responsible for the development of addiction. Thus, researches were conducted to establish an agonist that induces receptor internalisation, such as methadone. *Erythroxylum cuneatum* (EC), locally known as Chinta Mula, has various therapeutics properties including anti-diarrheal, anti-fever and anti-sinusitis. This study was designed to observe the effect of EC on receptor internalisation against chronic morphine. Human neuroblastoma cell line (SK-N-SH) was incubated with morphine for 24 hours before treated with methadone and EC at 0.1, 0.5, 1.0 $\mu\text{g/mL}$ for another 24 hours. The cell lysates were collected and proceed to protein determination procedure. Western blot technique was used to study the expression of G protein-coupled receptor kinases 2 (GRK2) and β^2 -arrestin while ELISA was used to determine the Protein kinase C (PKC). The data were analysed using IBM SPSS Statistics for One-way ANOVA and TukeyTM's multiple comparison tests. The expression of GRK2 and β^2 -arrestin were down-regulated while the level of PKC was up-regulated after chronic morphine ($P < 0.05$ vs control). Those expressions were normalised to the level of the control group after the treatment of methadone and EC ($p < 0.05$ vs morphine, $p > 0.05$ vs control). Methadone is an agonist that facilitates the internalisation of receptor. Methadone and EC were postulated to induce phosphorylation of the activated opioid receptor that was mediated by GRK2. The increased level of GRK2 thus subsequently recruits the β^2 -arrestin to the complex, hence responsible for receptor internalisation.

Keywords: *Erythroxylum cuneatum* (EC), morphine, G protein-coupled receptor kinases 2 (GRK2), Protein kinase C

ORA019

Effects of 2,6-bis-(4-hydroxyl-3methoxybenzylidene) Cyclohexanone or BHMC on the Migration and Invasion of Human Breast Cancer Cells

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The ability of the cancer cells to migrate and invade into the surrounding tissues has contributed to poor prognosis in cancer diagnosis. In order for the homing of the cancer cells to the new site, the cancer cells need to move and for the invasion to occur, the cancer cells was thought to form invadopodia to degrade the extracellular matrix. These are the crucial steps in cancer metastasis. Identification of a compound associated in hindering the migration and invasion of the cancer cells is important to produce anti-metastasis targeted therapy. 2,6-bis-(4-hydroxyl-3methoxybenzylidene) cyclohexanone or BHMC, a curcuminoid analogue has the potential to treat inflammation and hyperalgesia but to our knowledge, study of BHMC on migration and invasion cancer cells has yet to be explored. Thus, this study was conducted to determine the effects of BHMC on the migration and invasion of breast cancer cells. MDA-MB-231 human breast cancer cells were used as an *in vitro* model. MTT assay was carried out to find out the non-toxic concentrations of BHMC. These concentrations were being further used in all the assays conducted. The scratch migration assay was carried out to assess the percentage of the migrated distance of the breast cancer cells upon treatment with BHMC. The invasive behavior of MDA-MB-231 cells was investigated using transwell invasion assay (modified Boyden chamber assay) to evaluate the optical density representing the number of invaded cells. All data were statistically analyzed using one-way ANOVA followed by Post-Hoc Dunnett's Test. The results showed there is a significant reduction in percentage of migration when the cells were treated with BHMC ($p < 0.05$). The number of cells invaded through the collagen-coated transwell was also significantly reduced ($p < 0.05$) suggesting that BHCM may hinder the migration and invasion of breast cancer cells. BHMC is able to inhibit the migration and invasion of MDA-MB-231 human breast cancer cells can reduce the number of cells forming invadopodia in normal and even under hypoxic conditions.

Keywords: BHMC, breast cancer, invasion, metastasis, migration

ORA020

Non-synonymous Polymorphisms and Its Association with Obesity-related Traits and Cardiometabolic Risk Factors in Multi-ethnic Malaysian Adolescents

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Non-synonymous-mutation results in alteration of amino acid sequence of proteins. We examined the association between non-synonymous single-nucleotide-polymorphism (SNP) of selected genes with obesity-related-parameters and cardiometabolic risks among multi-ethnic adolescents across Central and Northern regions of Peninsular Malaysia. This cohort study recruited 1150 adolescents (96% 15-year olds, 38% boys, 79% Malays, 7% Chinese and 9% Indians) from 15 secondary schools in Kuala Lumpur, Selangor and Perak. Adiposity measures included were body mass index (BMI), waist circumference (WC), waist-and-hip-ratio (WHR) and percentage body fat (BF%) (Tanita SC-240MA). Cardiometabolic parameters included blood pressure, fasting glucose, and lipid profile. DNAs were collected from venous blood and isolated using GeneAII[®] DNA purification kit. Genotyping was performed using Sequenom MassARRAY. 14 SNPs were chosen from selected genes included ghrelin, leptin, melanocortin, ADRB3, INSR, ACE, FABP2, IGFBP1, PAPRG and SHBG. Comparison of parameters between genotypes was examined using Kruskal Wallis test. Multivariate logistic and linear regression were used to assess the relationship between genetic variants and adiposity and clinical parameters. SPSS 23 was used for analysis. The mean and standard deviations for obesity parameters in the adolescents were as follows: BMI=21.2 $\pm$ 5.1kg/m², WC=71.9 $\pm$ 11.7cm, WHR=0.8 $\pm$ 0.1 and BF%=24.2 $\pm$ 11.9%. Of the participants, 25% were overweight/obese (27% girls, 22% boys, 25% Malays, 25% Chinese and 25% Indians). Significant differences were observed between genotypes of ghrelin rs696217 and BMI (p=0.012), WC (p=0.002), BF% (p=0.04), systolic BP (p=0.02) and triglycerides (p=0.0004); and FABP2 and BF% (p=0.006). Those with rs696217 TT genotype were associated with increased risk of overweight/obesity (adjusted OR=2.25 95% CI 1.17-4.43, p=0.04) and higher BMI, WC, systolic BP and triglycerides level compared to GG genotypes (p<0.05). Other SNPs were not found to demonstrate significant associations with adiposity parameters or metabolic risks. In conclusion, amongst non-synonymous SNPs, ghrelin rs696217 was associated with increased risk of obesity and metabolic risks in our Malaysian adolescents.

Keywords: non-synonymous polymorphism, obesity, cardiometabolic, adolescents, ghrelin

ORA021

Phytochemical Screening and Identification of Contraceptive Related Phytochemicals of *Asparagus africanus* Lam. Using Gas Chromatography Mass Spectrometry (GC/MS)

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Asparagus africanus Lam is used traditionally in remedies as medicinal plant for treatment of various gastrointestinal disorders, headache, backache, stomach pain and for birth related uses. Therapeutic potentials of substances from different parts of the plant had been reported too, but only a few percentages have been fully elucidated. The aim of this study is to screen the root part of *A. africanus* Lam for the possible presence of bioactive contraceptive phytochemicals in its hexane fraction. The phytochemical analysis was carried out using gas chromatography mass spectrometry (GC/MS) and the obtained chromatograms were transferred to national institute of standards and technology MS search library for the possible compound detection and interpretable chemical and structural identification. Qualitative phytochemical screening were also carried out for tannins, flavonoids, alkaloids, saponins, and steroids. GC/MS analysis showed 11 peaks indicating the presence of 11 possible phytochemicals with likely different therapeutic functions. The major phytoconstituents with steroidal nucleus were stigmasterol, spirostan, tigogenin, and androstane. Furthermore, classical/manual phytochemical screening revealed the presence of flavonoids and saponins, but devoid of alkaloids and tannins. Based on the findings from this study, *A. africanus* contains some potential steroid compounds, which could explain the traditional uses of the root part of this plant as contraceptive, however this finding needs further pharmacological studies to confirm the contraceptive activity.

Keywords: *Asparagus africanus*, Asparagaceae, Phytochemical screening, Contraceptive, Gas chromatography mass spectrometry, Steroid

ORA022

A Double Blind Randomized Controlled Study to Evaluate the Efficacy of Different Doses of Oral *Channa Striatus* Extract among Primary Knee Osteoarthritis Patients

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Knee osteoarthritis (OA) is the leading cause of chronic disability at older age. *Channa striatus* (CS) is a fresh water fish and traditionally known for wound healing. A preliminary clinical trial had shown that CS has beneficial effect in the treatment of knee osteoarthritis (OA). To evaluate the efficacy of different doses of oral *Channa striatus* (Haruan) extract on primary knee osteoarthritis patients. Methodology: A randomized, double-blind, placebo-controlled 3-arm trial comparing oral CS extract 1000mg/day or 500mg/day and placebo among knee OA patients attending outpatient and orthopaedic clinics Universiti Sains Malaysia Hospital for 6-month intervention period was conducted. The main outcome measures were Western Ontario and McMaster University Osteoarthritis Index (WOMAC) and analgesic score. Laboratory based blood tests were used as safety measures. One hundred and twenty patients were randomized and 112 patients were included in the intention-to-treat analysis. There were significant improvement of stiffness and physical function at month 6 between CS 500mg/day vs. placebo ($p < 0.005$) and CS 1000mg/day vs. placebo ($p < 0.005$). There was no significant difference for analgesic score. The safety profiles were not significant. Both doses of CS showed similar efficacy and more effective than placebo in treating the symptoms of knee OA.

Keywords: Knee osteoarthritis, *Channa striatus*, symptoms, pain

ORA023

Optimization of Solid Lipid Nanoparticles Formulation for Oral Delivery of Acyclovir

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Acyclovir is an antiviral drug commonly used to treat Herpes Simplex Virus (HSV) infection. However, its oral bioavailability and absorption are very low due to its poor solubility. The half-life of acyclovir is also very short which runs about 2.5 to 3 hrs. Hence, patients are prescribed with high doses of acyclovir for its effectiveness, but will experience unwarranted adverse effects due to high doses intake. Acyclovir is therefore in need of a suitable drug carrier that could improve its current pharmacokinetic limitations. In this study, we investigated the effectiveness of solid lipid nanoparticles dispersion loaded with acyclovir for oral administration. Response Surface Methodology (RSM) method was utilized with the aims to optimize the formulation developed using two different types of plant-based solid lipid, i.e., Biogapress Vegetal BM 297 ATO (glyceryl dipalmitostearate) and Compritol 888 ATO (glyceryl dibehenate) and evaluate the influence of the main nanoparticles composition on the physicochemical properties of the nanocarrier. Particles morphology, size, polydispersity Index (PDI) and zeta potential were characterized. Results showed that both nanoparticles fabricated were in spherical-shaped with mean particle sizes of 104.89 ± 5.53 nm (compritol) and 122.72 ± 2.15 nm (vegetal), which were within the predicted size. The polydispersity index of compritol and vegetal were 0.21 ± 0.01 and 0.23 ± 0.01 and zeta potential were -37.00 ± 0.89 mV and -24.37 ± 1.07 mV, respectively, which showed that good dispersion of nanoparticle suspensions were achieved. These outcomes indicated that both types of solid lipid nanoparticles could potentially be exploited as a delivery system for acyclovir.

Keywords: solid lipid nanoparticles; acyclovir; Response Surface Methodology

ORA024

***Labisia Pumila* Regulates the Expressions of Bone-related Genes and Pro-inflammatory Cytokines in Postmenopausal Osteoporosis Rat Models**

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Labisia pumila var. *alata* (LP) has shown potential as an anti-osteoporotic agent in recent years. The crude extract of LP was reported to reverse trabecular microarchitecture changes induced by ovariectomy. The mechanism is still unclear but it may be elucidated by examining the bone molecular pathways. This study aimed to evaluate the bone-related genes and pro-inflammatory cytokines expressions to provide a mechanistic overview on how the different LP extracts could prevent degenerative bone changes. Forty-eight female Sprague-Dawley rats were randomly divided into sham-operated (Sham), ovariectomized control (OVX), ovariectomized and given oestrogen at 64.5 µg/kg (ERT), ovariectomized and given LP aqueous extract at 100 mg/kg (LPaq), ovariectomized and given LP methanol extract at 100 mg/kg (LPmet) and ovariectomized and given LP ethanol extract at 100 mg/kg (LPet). All treatments were given daily via oral gavages for nine weeks. Rats were then euthanized and femora dissected out for genes and cytokines expressions analysis. Among the extracts, LPaq was found to produce the highest expressions of OPG, osteocalcin, osterix, osteonectin and ALP. LPaq was also shown to down-regulate the expressions of RANKL, MMP9, M-CSF as well as cytokine IL-1 β . Aqueous extract is the best extract of LP which may exert anti-osteoporosis activity by regulating the bone-related genes and cytokines expressions.

Keywords: *Labisia pumila*; osteoporosis; postmenopausal, bone; gene expression; cytokine

ORA025

Comparative Analysis of the Six Human Karyopherin Alpha Promoters: Availability of Nuclear Receptors Binding Sites

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Introduction: The transport of the nuclear receptor (NR) family of ligand-activated transcription factors is controlled by karyopherins (KPNA). Karyopherins are nuclear import factors that interact with cargo proteins (such as nuclear receptors) containing nuclear localisation signal and mediates their import into the nucleus. The KPNA family of adapter proteins form a molecular bridge between these nuclear cargoes and nuclear import machinery. Six KPNA encoding genes have been identified in human and evidence show that these proteins show cargo specificity. To date, no comparative study has been conducted to compare the six human karyopherins or even elucidate any putative nuclear receptor binding sites within them which would explain its specificity towards a certain cargo. **Objective:** To examine the association of NR-dependent regulation of human KPNA promoters using *in silico* analysis. **Methodology:** *In silico* analysis was conducted using three software namely NCBI, mVISTA and Mat Inspector to find the promoter region of the six human KPNA followed by identifying the NR binding sites within these KPNA promoters. The NCBI gene database was first used to retrieve the KPNA mRNA sequence for human and three other species. The region acquired was further manipulated to obtain approximately 20kb of promoter region upstream of the mRNA sequence. Following that, the 20kb sequence of the human KPNA gene was selected as the reference sequence and aligned against equivalent region in the pre-determined species using VISTA analysis. Once the promoter position has been identified, Mat Inspector software was employed to determine the putative nuclear receptor binding sites within the entire human KPNA promoter region. **Results:** *In silico* analysis aided in identifying the promoter region of the six human KPNA and the available NR binding sites within it. Interestingly, some but not all KPNA promoters shared the same NR while others possessed multiple binding sites for the same NR. **Conclusion:** The association of NR and human KPNA was demonstrated using *in silico* analysis, however, the impact of NR in regulating the human KPNA expression warrants further investigation.

Keywords: Karyopherin alpha, nucleocytoplasmic shuttling, nuclear receptor, *in silico* analysis

ORA026

Exogenous Leptin Administration Does Not Affect Mnng-induced Tumourigenesis in the Stomach of Female Sprague-dawley Rats

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N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) is used to induce adenocarcinoma in the stomach of rats. Leptin and its receptors have been found in the stomach of rats and humans. Although leptin has been shown to aid ulcer healing in the stomach, its impact on tumour formation in the stomach has not been examined before. This study therefore examined the effects of leptin on MNNG-induced tumourigenesis in the stomach of female Sprague-Dawley rats. Six-week old female rats were divided into 4 groups (n=6). Group 1 served as a control. Group 2 was given 100 µg/ml of MNNG in drinking water daily. Group 3 was given 100 µg/ml of MNNG in drinking water and intraperitoneal injection of 60 µg/kg of leptin daily. Group 4 was given intraperitoneal injection of 60 µg/kg/day of leptin daily. Half the rats were euthanized after 20 weeks and the other half at 40 weeks. Stomachs were collected for histopathological and gene expression studies. Expressions of ARID1A, E-Cadherin, FAT4, Lmyc, APC, PGC, PPARG, TFF1, TFF2 in the stomach were determined using RT-PCR. Data were analysed using one-way ANOVA. Histological examination of the stomach did not show any pathological lesion in any of the 4 groups. E-Cadherin and APC expressions were lower and PGC expression was higher in MNNG-treated rats. E-Cadherin and APC expressions were lower but TFF2 expression was higher in leptin-treated rats. PGC expression was lower in MNNG-treated group. There was no significant difference in the expression of other genes. It appears that leptin neither protects nor facilitates MNNG-induced tumourigenesis in the stomach of the rat. The absence of any significant lesion following MNNG treatment might also be due to the resilience of female rats, as estrogen has been shown to decrease the progression of gastric cancer by inhibiting erbB-2 oncogene expression.

Keywords: MNNG, leptin, rat, PCR, tumourigenesis

ORA027

A Novel Multiplex Pcr-rflp Protocol for Simultaneous Detection of Cyp3a4*4 A>g, Cyp3a4*18b G>a And Cyp3a4*22 C>t

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Single nucleotide polymorphisms (SNPs) in CYP3A4 enzymes may result in functional changes that affect the activity. The objective of this study is to develop a novel multiplex polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method to determine the allelic frequencies of CYP3A4*4 (rs55951658), CYP3A4*18B (rs2242480) and CYP3A4*22 (rs35599367) in breast cancer patients. Postmenopausal breast cancer patients (n=94) were recruited and blood (1.0 ml) was taken for DNA extraction. Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was conducted. The primers were designed using Primer3 software with primer specificities checked using the BLAST database. The primer specificity, functionality and annealing temperature were investigated using uniplex PCR protocols, followed by a single multiplex PCR-RFLP method. The digested amplification fragments were analyzed by a gel electrophoresis (4%) and subsequently validated by sequencing. Amplification of CYP3A4*4 yielded a band of 244 bp. Digestion with BsmAI yielded 15 bp, 88 bp and 141 bp for the wild type. No variant allele of CYP3A4*4 was detected in the samples. The PCR product for CYP3A4*18B was 331 bp and its digestion with RsaI yielded 115 bp and 216 bp for the wild type; 115 bp, 216 bp and 331 bp for the heterozygous and 331 bp for the homozygous variants. The PCR product for CYP3A4*22 was 793 bp and its digestion by BseYI yielded 219 bp and 793 bp for the wild type. No variant allele of CYP3A4*22 was detected in the samples. Our study is the first to report on CYP3A4*18B allele in Malaysian subjects. A simple, cost-effective and time-saving multiplex PCR-RFLP protocol that can be routinely applied in the identification of SNPs as well as the determination of the allelic and genotypic frequencies of CYP3A4*4, CYP3A4*18B and CYP3A4*22 has been successfully developed.

Keywords: Multiplex PCR-RFLP; CYP3A4*4, CYP3A4*18B; CYP3A4*22

ORA028

The Combination of Gamma-tocotrienol and 13-cis Retinoic Acid to Treat Neuroblastoma Cell Lines is Synergistic.

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Researchers found that gamma-tocotrienol (γ T3) induces apoptosis in neuroblastoma SH-SY5Y cells by binding to the BH3 groove of Bcl-2. It has also been investigated for its synergistic effects when used in combination with other drugs. 13-*cis* retinoic acid (13cRA) is used as a differentiation agent in the maintenance stage of high-risk neuroblastoma treatment, to reduce recurrence of malignant tumours. High-risk neuroblastoma mainly affects children and toddlers and is known to be resistant to common treatment (surgery and chemotherapy), frequently due to amplified MYCN, considered a risk factor in high-risk neuroblastoma. The cell lines we use are SH-SY5Y and SK-N-BE(2); SH-SY5Y has normal MYCN expression but SK-N-BE(2) has amplified MYCN. This study aims to further investigate the mechanism of action by which γ T3 induces apoptosis and also explore the potential for a synergistic effect of γ T3 and 13cRA used in combination on neuroblastoma cell lines. We treated SH-SY5Y and SK-N-BE(2) cell lines with γ T3 and/or 13cRA and measured cell viability and cell death. We found that while individual treatments produced a significant reduction in cell viability and increase in cell death, the addition of γ T3 reduced the IC₅₀ of 13cRA by more than half in both cell lines (37.7 μ M 13cRA to 15 μ M in SH-SY5Y cells and 43.4 μ M 13cRA to 20 μ M in SK-N-BE(2) cells). Calculated combination index (CI) values <1 indicate that the reduction in cell viability when using a combination of γ T3 and 13cRA is considered synergistic. Based on these results, we can conclude that there is a synergistic effect when γ T3 is combined with 13cRA to treat neuroblastoma cell lines. Currently, expression of genes of interest (BCL2, BCLXL, MYCN, CASP3 and CASP9) is being investigated using quantitative real time PCR. Further studies to investigate protein expression using Western blot, and an in vivo xenograft study on mice are planned.

Keywords: gamma-tocotrienol, Bcl-2, apoptosis, neuroblastoma

ORA029

Cytotoxic Effects of the Dual ErbB Tyrosine Kinase Inhibitor, Lapatinib, on Tumour and Intestinal Cell Lines

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Lapatinib, an ErbB1/ErbB2 tyrosine kinase inhibitor (TKI) is effective in breast cancer treatment but is associated with diarrhoea. ErbB1 inhibition by lapatinib may interfere with the normal functioning in the intestines. This study aimed to determine the cytotoxic properties of lapatinib on rat breast carcinoma (Walker 256) and intestinal epithelial (IEC-6) cells and to evaluate the relationship between ErbB1 expression and sensitivity to growth inhibition by lapatinib. The cytotoxic effect of lapatinib on Walker 256 and IEC-6 was evaluated via XTT assay and FACS analysis. Cell lines were incubated with lapatinib for 6, 24 or 48 hours before evaluation. ErbB1 and ErbB2 mRNA and protein expression were determined via RT-PCR and immunofluorescence staining, respectively. Lapatinib inhibited 50% Walker 256 and IEC-6 cell growth at 8.2 ± 0.21 and $3.0 \pm 0.49 \mu\text{M}$ respectively. Higher percentage of necrotic cells were observed in lapatinib-treated Walker 256 ($38.05 \pm 10.00\%$) compared to control untreated cells ($11.86 \pm 7.95\%$) ($p < 0.05$), at 48 hours. Lapatinib-treated IEC-6 at 24 hours showed higher percentage of late apoptotic cells ($43.7 \pm 14.04\%$) compared to controls ($13.86 \pm 2.68\%$) ($p < 0.05$). At 48 hours, lapatinib-treated IEC-6 showed higher percentage of late apoptotic cells ($59.74 \pm 11.15\%$) ($p < 0.05$) compared to controls ($21.22 \pm 12.73\%$). ErbB1 mRNA was unable to be detected in Walker 256 due to low expression. However, ErbB1 and ErbB2 protein staining were detected in both cells. Lapatinib exhibited cytotoxic properties on ErbB1/ErbB2 expressing cell lines, with intestinal cells being more sensitive to lapatinib compared to tumour cells. Lapatinib induced necrosis in tumour cells, while inducing late apoptosis in intestinal cells may explain lapatinib-induced diarrhoea in patients administered with the drug which could be due to apoptosis of intestinal epithelial cells leading to barrier disruption and consequently diarrhoea. A link between ErbB1 expression and diarrhoea was not found by these studies. However, much remains to be learned on the molecular mechanisms related to lapatinib's cytotoxic effect.

Keywords: Lapatinib, ErbB1/ErbB2 TKI, Walker 256, IEC-6, diarrhoea

ORA030

Comparing the Analgesic Activities of Existing Drugs for the Treatment of Neuropathic Pain.

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Neuropathic pain originates from lesion of somatosensory system, either centrally or peripherally. Allodynia and hyperalgesia are symptoms often experienced by neuropathic pain patients. The objective of the present study was to compare the analgesic activity of carbamazepine, gabapentin and amitriptyline in neuropathic pain mice model. Chronic constriction injury (CCI) on sciatic nerve attempts to induce symptoms like neuropathic pain in animal model to mimic human condition. Behavioral tests were conducted on male ICR mice using von Frey filament, Randall-Selitto and Hargreaves tests. Although all three drugs displayed analgesic activity, the effects varied according to dosage and behavioral tests. Carbamazepine significantly reduced mechanical hyperalgesia while gabapentin displayed analgesic activity against mechanical hyperalgesia, however it was not significant against thermal hyperalgesia. Amitriptyline significantly reduced tactile allodynia and displayed significant inhibition of mechanical hyperalgesia. This study demonstrated dissimilarity in analgesic effects of carbamazepine, gabapentin and amitriptyline against tactile allodynia, mechanical hyperalgesia and thermal hyperalgesia in CCI-induced neuropathic pain.

Keywords: neuropathic pain, chronic constriction injury, carbamazepine, gabapentin, amitriptyline

ORA031

Protective Role of Tocotrienol-rich Fraction Supplementation on Oocytes Retrieved from Aging Mice

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A decline in female fertility is attributed to aging. Accumulation of reactive oxygen species with age will lead to excessive oxidative stress which eventually will produce a negative impact on the female reproductive system. On the other hand, tocotrienol, a potent antioxidant has been proven to exhibit a protective role against the harmful effects of excessive free radicals. Thus, objective of this study were to determine the effect of tocotrienol supplementation in aging mice on the i) quality of embryos and ii) the DNA damage of oocytes as well as 2-cell stage embryos. In this study, young female mice at the age of six weeks old (Group 1) and aging eight months old mice were used (Group 2). Two groups of six months old mice were used; one group was given corn oil as vehicle control (Group 3) and another group was given tocotrienol-rich fraction (TRF) supplementation orally at the dose of 150 mg/kg for two months (Group 4). At the end of TRF-supplementation period, mice were superovulated and euthanized to collect the oocytes and 2-cell stage embryos for quality assessment. Oocytes and embryos retrieved were further analysed to determine the degree of DNA damage by using comet assay. Results showed that there was a significant reduction on the quality of embryos in aging mice (Group 2) as compared to young group (Group 1) whereas no significant different in the quality of embryos in TRF-supplemented mice (Group 4) as compared to its control (Group 3). The percentage of DNA damage in oocytes retrieved from Group 2 were significantly higher ($p < 0.05$) as compared to oocytes from Group 1. Similarly, DNA damage in 2-cell embryos were significantly higher in Group 2 ($p < 0.01$) as compared to Group 1. Interestingly, TRF-supplementation in Group 4 was able to reduce the percentage of DNA damage in oocytes ($p < 0.05$) as compared to its control, Group 3 but not in embryos. Therefore, it is suggested that TRF-supplementation is able to delay the consequences of aging leading to infertility by reducing the DNA damage in the oocytes.

Keywords: oocytes, embryos, DNA damage, tocotrienol, aging mice

ORA032

Ameliorative Effect of Malaysian Propolis on Changes in Antioxidant Enzymes and Reproductive Hormones Levels in Streptozotocin-Induced Diabetic Female Rats

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To determine the effects of ethanol extract propolis (EEP) on plasma antioxidant enzymes and reproductive hormones levels in streptozotocin-induced diabetic female rats. Design and Forty female rats (8-10 week old; weighing 190 – 220 g) were assigned into five groups (n= 8/group) i.e. non-DM group on 0.5 ml/day distilled water, DM group on 0.5 ml/day distilled water, DM+300EEP group on 300 mg/kg/day EEP, DM+600EEP group on 600 mg/kg/day EEP and DM+metformin group on 100 mg/kg/day metformin. Type 1 diabetes was induced using streptozotocin (60 mg/kg) intraperitoneally and treatments were given by oral gavage for four weeks. Initial and final fasting blood glucose (FBG) levels were recorded, and rats were sacrificed after 4 weeks at dioestrus phase, Blood samples were taken for FBG levels, plasma insulin and antioxidant enzymes activity. The FBG level was significantly higher while plasma insulin, superoxide dismutase, catalase, follicle-stimulating hormone, luteinising hormone and oestradiol levels were significantly lower in DM group compared with non-DM group. However, the plasma insulin, superoxide dismutase and catalase were significantly higher while FBG was lower in DM+300EEP and DM+600EEP groups compared with DM group. Significantly higher follicle-stimulating hormone and luteinising hormone levels were found in DM+600EEP compared with DM group. These findings suggest that propolis possesses antioxidant property and improves reproductive hormones levels in streptozotocin-induced type 1 diabetic rats. Further research is needed on its mechanism of action and other effects on reproductive organs.

Keywords: antioxidant enzymes, diabetes, propolis

ORA033

Knowledge, Attitude and Practice of Traditional, Complementary and Alternative Medicine (T&CAM) Among Antenatal and Postnatal Women

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This study was aimed to determine knowledge, attitude and practices of T&CAM by women during pregnancy and after delivery and its correlation to the socio demographic factors. This cross-sectional study was conducted at a mother and child health clinic in Perak. Minimum sample size was calculated as 97 assuming that 50% will have good knowledge with a precision of 10% for 95% CI. Data were collected from 103 antenatal and postnatal mothers registered at the health clinic using structured questionnaire, set in four different sections. Section 1 included general information and Section 2, 3 and 4 included questions to assess their knowledge, attitude and practice respectively. Data were analyzed using SPSS version 16.0. The participants included antenatal (66.02%) and postnatal (33.98%) women. The age of the participants ranged between 20 to 59 years and the mean age was 29.72 years. The knowledge of the participants regarding T&CAM varied between 16.50% and 96.12% depending on the questions. A significant association was found between knowledge and occupation (p 0.039). As regards to attitude, 98 (95.15%) of the total respondents were having good attitude. A total of 39 (37.86%) respondents strongly agreed that one should consult a doctor before taking any traditional herbal medications during pregnancy or after delivery. There were about six types of T&CAM were practised by study participants. From the total respondents, 27% were using both T&CAM and conventional medicine whereas 73% used only conventional medicines prescribed by the doctors. Diet was the most common T&CAM (33.9%) practised. Women attending maternal and child health clinic had good knowledge and positive attitude towards the usage of T&CAM during antenatal and postnatal period but majority were using only conventional medicine prescribed by doctors.

Keywords: T&CAM, Antenatal and Postnatal Women

ORA034

Royal Jelly Improves Reproductive Hormones Levels and Oestrus Cycle in Hyperandrogenised Female Rats

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To determine the effects of royal jelly (RJ) on reproductive hormones levels and oestrus cycle in hyperandrogenised female rats, a model for polycystic ovarian syndrome. Forty immature female rats (three weeks old, 40-50 g) were randomly divided into 5 groups i.e. Control, Testosterone (T), T+100RJ (100 mg/kg/day RJ), T+200RJ (200 mg/kg/day RJ) and T+400RJ (400 mg/kg/day RJ). Hyperandrogenic state was induced by giving intraperitoneal injection of testosterone propionate for three weeks followed by RJ via oral gavage daily for four weeks. Vaginal smear was done daily for assessment of oestrus cycle. At the end of the study, all rats were sacrificed and blood was collected for reproductive hormones levels assessment. Testosterone and oestradiol levels were significantly higher while follicle-stimulating hormone level was significantly lower in T group compared to control group. In T+100RJ group, oestradiol level was significantly lower compared to T group. In T+200RJ group, follicle-stimulating hormone level was significantly higher while luteinizing hormone, testosterone and oestradiol levels were significantly lower compared to T group. Meanwhile in T+400RJ group, testosterone and oestradiol levels were significantly lower compared to T group. The percentage of regular oestrus cycle was significantly lower in T group compared to control and T+200RJ groups. These findings may suggest that RJ at the dose of 200 mg/kg/day is the best dose in improving reproductive hormones and oestrus cycle in hyperandrogenised female rats, which need further study to evaluate its exact mechanism of action.

Keywords: Royal jelly; hyperandrogenism; oestrus cycle

ORA035

Effect of *Marantodes Pumilum* on Uterine Contraction in Post-partum Rats

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M. pumilum has been used as a uterotonic agent, however mechanisms remains unknown. In this study, we investigated effect of this herb on uterine contraction and the mechanisms involved. Study was conducted in-vitro using uterus of estrogenized, intact rats and in-vivo using uterus from post-partum rats fed with *M. pumilum* aqueous extract at 100, 250 and 500 mg/kg/day for seven consecutive days. For in-vitro study, effects of Ca²⁺ channel and uterotonic receptor inhibitors on *M. pumilum*-induced uterine contraction were investigated. For in-vivo study, expression of contractile proteins (MLCK, SERCA, and CaM), Ca²⁺-signalling proteins (IP3K, G $\hat{1}\pm$ and G $\hat{1}^2$), uterotonic receptors and estrogen receptors in uterus were quantified and their distribution was determined. LC-MS was used to identify compounds present in the extract. Administration of *M. pumilum* aqueous extract either in-vitro or in-vivo increases force of uterine contraction. In-vitro study shows the force was reduced following co-administration of uterotonic receptor antagonists (atropine, atosiban and AL-8810), cyclo-oxygenase inhibitor (indomethacin), Ca²⁺-channel blockers (nifedipine and thapsigargin), histamine, inositol triphosphate inhibitor (2-APB), removal of extracellular Ca²⁺ and placing the uterus in a Ca²⁺-free solution. Meanwhile, in post-partum rats receiving 500 mg/kg/day *M. pumilum* aqueous extract, progesterone levels decreased with higher expression of contractile proteins (MLCK, SERCA, and CaM), Ca²⁺-signalling proteins (IP3K, G $\hat{1}\pm$ and G $\hat{1}^2$), uterotonic receptors (M2, PGF2 $\hat{1}\pm$ and oxytocin) and estrogen receptors in myometrium. LC-MS shows the presence of several active compounds that might exert these effects. *M. pumilum* justify its use as uterotonic agent particularly in the post-partum period.

Keywords: *Marantodes Pumilum*, uterus, contraction, post-partum

ORA036

Exercise Capacity and Substrate Oxidation in Triathletes.

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Anthropometry plays an important role in determining the measures of performance. Triathletes are in a unique position with respect to the relationship between anthropometry and performance since triathlon involves running, cycling and swimming. Thus we proposed to characterize physiological measures of performance as well as energy metabolism in triathletes. Eight male elite triathletes of Chinese origin with an average age of 18.50 ± 2.98 years took part in this study. An incremental exercise test using the Bruce Protocol was carried out to measure the maximal oxygen uptake (VO₂max) and ventilatory threshold (VT). From these measures the rate of fat oxidation (Fox) and maximal fat oxidation (Fatmax) of the athletes was calculated. Descriptive statistical analysis was performed using SPSS version 21. The mean VO₂max was 65.29 ± 4.91 ml/kg/min, with the VT achieved at a VO₂max of 51.31 ± 7.29 ml/kg/min. The fat oxidation rate was 0.45 ± 0.15 g/min with a Fatmax of 40.13 ± 9.48 . We compared these findings through a literature search with age-matched triathletes from other ethnic background and found that our triathletes had comparable VO₂max and VT. However we found our triathletes achieved higher rate of fat oxidation. We conclude that though ethnicity may play a role in anthropometry and therefore affects physiological measures of performance; it doesn't seem to affect VO₂max and VT. However it does seem to play a role in the body's preference of metabolic substrate during a strenuous exercise.

Keywords: exercise performance; triathletes; ventilatory threshold; fat oxidation; VO₂max

ORA037

Effect of Dexamethasone on Production and Degradation of Fibronectin and Alpha Smooth Muscle Actin: In Vitro Study on Human Trabecular Meshwork Cells

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Corticosteroid treatment is commonly associated with increased intraocular pressure due to accumulation of extracellular matrix (ECM) in trabecular meshwork (TM). Deposition of ECM components such as fibronectin (FN) and alpha smooth muscle actin (α -SMA) are caused by increased ECM production or reduced ECM degradation or both. Objective: This study was aimed to evaluate time-depended effect of dexamethasone on production of FN, α -SMA, and MMP-2 by cultured human TM (HTM) cells. Primary HTM cells were divided into three groups: Group 1 was cultured in Dulbecco's modified Eagle's medium (DMEM) only; groups 2 in DMEM with 0.1% DMSO and group 3 in DMEM with dexamethasone 100 nM dissolved in 0.1% DMSO. Cells were incubated for 7, 14 and 21 days. Immunocytochemistry was done to visualize the extent of ECM deposition and ELISA was done for quantal estimation tested parameters. FN concentration measured by ELISA was found to be 1.33, 1.35 and 1.38 folds higher ($p < 0.05$) in dexamethasone treated group compared to DMEM group at day 7, 14 and 21 of the treatment respectively. Concentration of α -SMA was 1.64, 1.60 and 1.94 fold higher ($p < 0.05$) in cells treated with dexamethasone compared to DMEM. No significant difference of FN and α -SMA was observed between dexamethasone treated groups at 3 time points. Immunofluorescent staining results were in line with Elisa and showed increased secretion of both FN and α -SMA due to dexamethasone exposure. Concentrations of both total and active MMP-2 were significantly lower in the dexamethasone group compared to DMEM treated group at 3 time points. Dexamethasone significantly increases deposition of both FN and α -SMA however those productions do not increase beyond the first week of dexamethasone exposure. Dexamethasone induced reduction of MMP-2 may attribute to ECM deposition.

We acknowledge the financial support from the grant 600-RMI/FRGS 5/3 (24/22014).

Keywords: Dexamethasone, Fibronectin, Alpha Smooth Muscle Actin, Trabecular Meshwork Cells, In Vitro

ORA038

The Effect of Dexamethasone on the Deposition of Collagen Type I, III and IV by Cultured Human Trabecular Meshwork Cell

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Therapeutic use of glucocorticoids such as dexamethasone (DEX) is associated with elevated intraocular pressure (IOP), which may progress to optic neuropathy and irreversible blindness. Steroid-induced oculohypertension is associated with increased deposition of extracellular matrix (ECM) components especially collagen (COL) types I, III and IV in the trabecular meshwork (TM) causing increased aqueous humor outflow resistance and increased IOP. This study aimed to evaluate time-dependent effect of DEX on COLI, COLIII and COLIV deposition by human TM cells (HTMC). Three groups of primary HTMC were cultured in low-glucose Dulbecco's modified Eagle's medium (DMEM); DMEM containing DEX (100 nM) dissolved in 0.1% DMSO and DMEM containing 0.1% DMSO, respectively. The incubation was done for 7, 14 and 21 days. Subsequently COLI, COLIII and COLIV expression was estimated using ELISA and immunocytochemistry. ELISA showed that the COLI expression in the culture media was 4.72, 6.26 and 5.21 folds higher in DEX-treated group compared to DMEM-treated at 7, 14 and 21 days, respectively. COLIII expression on days 7, 14 and 21 increased by 1.63, 1.67 and 2.74 folds, respectively, in DEX-treated group compared to DMEM-treated. In DEX-treated group, COLI and COLIII were significantly higher on days 14 and 21 compared to day 7 ($p < 0.05$) with no significant difference between days 14 and 21. COLIV expression was 1.07, 1.65 and 1.66 folds higher in DEX group compared to DMEM group with no significant differences at three time-points. Qualitative and quantitative estimations by immunostaining were also in accordance with those of ELISA. Secretion of COLI, COLIII and COLIV by HTMC significantly increases after exposure to DEX over 21 days and this effect on COL I and COL III secretion is time-dependent.

We acknowledge the financial support under grant numbers 600-RMI/FRGS TD 5/3 (2/2015), 600-RMI/FRGS 5/3 (110/2014) and 600-RMI/FRGS 5/3 (24/2014).

Keywords: Trabecular Meshwork Cells, Collagen I, Collagen III, Collagen IV, Dexamethasone

ORA039

Dose-dependent Effect of Trans-resveratrol On Collagen Secretion by Cultured Human Trabecular Meshwork Cell

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Elevated intraocular pressure (IOP) in steroid-induced glaucoma results from increased deposition of extracellular matrix (ECM) components such as collagens in trabecular meshwork (TM). Trans-resveratrol was previously shown to reduce IOP in rats; however, its effects on ECM deposition in TM remain unknown. Aim: To evaluate the dose-dependent effect of trans-resveratrol on collagen types I, III and IV deposition by human TM cell (HTMC). HTMC were cultured in low-glucose Dulbecco's modified Eagle's medium (DMEM) and were treated with trans-resveratrol in concentrations of 3.125, 6.25, 12.5 and 25 μM for 2 days in the presence of dexamethasone (100 nM) (TR groups). Cells in control groups were cultured in DMEM alone (DMEM group) or DMEM containing dexamethasone (100 nM) (DEX group). Collagen types I, III and IV were estimated in media using ELISA. Collagen I, III and IV concentrations were significantly higher in DEX compared to DMEM group. However, collagen I concentration in TR 3.125, 6.25, 12.5 and 25 groups was lower by 1.34, 1.35, 1.43 and 1.43 folds, respectively, compared to DEX group and the difference was significant for 12.5 and 25 μM groups. Collagen III concentration was 1.59, 1.83, 1.64 and 1.83 fold lower in TR 3.125, 6.25, 12.5 and 25 groups, respectively, compared to DEX group but the difference was significant for TR 6.25 and 12.5 groups. Collagen IV concentration in any of the TR groups did not differ from DEX group. When compared to DMEM group, TR 12.5 group showed significantly lower collagen I but not collagen III and IV. None of the other TR groups showed differences from DMEM group for any collagen subtype. Trans-resveratrol (12.5 and 25 μM) significantly reduces secretion of collagen I and III by dexamethasone-treated HTMC. Financial support under grants 600-RMI/FRGS TD 5/3(2/2015), 600-RMI/FRGS 5/3 (110/2014), 600-RMI/FRGS 5/3 (24/22014) is acknowledged.

Keywords: glaucoma, dose dependent trans-resveratrol, Dexamethasone, ECM deposition, Collagen

ORA040

Effect of Resveratrol on the Viability of Human Trabecular Meshwork Cells (Htmcs)

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Resveratrol, a polyphenol found in grapes and berries, has been shown to possess significant anti-oxidant, and anti-apoptotic effects and hence has been investigated for several therapeutic applications. Resveratrol can increase cell proliferation at lower doses and induce apoptosis at higher doses. We investigated its effect on the viability of trabecular meshwork (TM) cells in the presence and absence of dexamethasone since it has been shown to affect TM structure and function in rats with steroid-induced oculohypertension. Human TM cells (HTMCs) from ScienCell Research Laboratories were cultured in Dulbecco's Modified Eagle Medium (DMEM) till 90% confluency. Cells were then cultured in 96-well plate for 2, 5, and 7 days. Culture was done in DMEM (control group), DMEM containing trans-resveratrol (3.125, 6.25, 12.5, 25, and 50 μ M) dissolved in 0.1% DMSO and DMEM containing trans-resveratrol (3.125, 6.25, 12.5, 25, and 50 μ M) and dexamethasone (100 nM) dissolved in 0.1% DMSO. Experiment was done in 3 biological and 3 technical replicates. Cell viability was assessed by using MTS assay. Based on percentage of cell survival, cytotoxic concentration 50 (CC50) was calculated for 3 time-points. After 2, 5 and 7 days of treatment, the CC50 of trans-resveratrol for HTMCs was 57.4, 53.6 and 57.8 μ M, respectively. In the presence of dexamethasone, the CC50 of trans-resveratrol at 2, 5 and 7 days of treatment was 105.3, 108.1 and 67.1 μ M, respectively. Maximum non-toxic concentration for trans-resveratrol, with and without dexamethasone, ranged between 3.125 to 25 μ M after 5 and 7 days of treatment, but was slightly lower after 2 days of treatment. At concentrations of more than 25 μ M, trans-Resveratrol causes cytotoxic effect on HTMC, regardless of the time of treatment.

Keywords: trans-Resveratrol, viability, CC50

POS001

In Vivo Effect of *Piper Sarmentosum* Methanolic Extract on Stress-Induced Gastric Ulcers in Rats

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Piper sarmentosum ((Piperaceae) leaves are traditionally used by the Asians to treat numerous common ailments including asthma, headache, fever and gastritis. To determine and compare the effects of *Piper sarmentosum* (PS) with omeprazole (OMZ) on gastric lesions, gastric acidity, gastric malondialdehyde (MDA) and prostaglandin E2 (PGE2) content in rats exposed to restraint stress. The methanolic extract of PS was prepared in the dose of 500 mg/kg. Twenty-eight male Wistar rats were randomly assigned into 4 equal sized groups; two control groups and two treated groups which were supplemented with either PS or OMZ orally at a dose of 500 mg/kg and 20 mg/kg body weight respectively. After 28 days of treatment, one control group, the PS and OMZ group were subjected to a single exposure of water-immersion restraint stress for 3.5 hours. After the last exposure to stress, the stomach was exercised for the evaluation of the parameters. Oral supplementation of PS was as effective in preventing the formation of gastric lesion when compared with OMZ. The increased gastric acidity and MDA due to stress was also reduced with supplementation of PS and OMZ. Only PS had the ability to reduce prostaglandin E2 loss and have the ability to down regulate cyclooxygenase-2 (COX-1) mRNA expression with stress exposure. *Piper sarmentosum* possesses a similar protective effect against stress-induced gastric lesions with omeprazole. The protective effect was associated with decreased lipid peroxidation, increased PGE2 and reduction in gastric acidity and reduction in COX-2 mRNA expression which was altered by stress.

Keywords: *Piper sarmentosum*, gastric ulcers, restraint stress, prostaglandin, lipid peroxidation

POS002

Neuroprotective Effect of Malaysian Tualang Honey in an Experimental Rat Model of Alzheimer's Disease (AD)

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To investigate the neuroprotective effect of Malaysian Tualang honey in chronic cerebral hypoperfusion-induced neurodegeneration in rats and cognition enhancing potential of honey. Study of Alzheimer's disease (AD) in rat-animal model is achieved by inducing chronic cerebral hypoperfusion through permanent ligation of the common carotid arteries (2 vessels occlusion- 2VO). 40 male Sprague-Dawley (weighing 250-300 gm) rats were randomly divided into 4 groups; SHAM, untreated 2VO and honey treated 2VO & honey treated. Honey was administered orally (1.2mg/kg) 10 days before 2VO and daily up to 10 weeks. Various Morris water maze (MWM) behavioural tasks were conducted in this study. It involved reference memory, working memory and relearning tasks for short and long term memory assessment. It also included cued version phase to detect sensorimotor dysfunction and visual impairment in animal models after 2VO. The animals from groups were again divided into Memory Group (n=5) and Learning Group (n=5). The memory group animals were assessed for the long term memory whilst the learning group animals were tested for short term memory and relearning. Data was analyzed using one-way ANOVA and presented as means $\pm$ SEM. $P < 0.05$ is considered as significant. This study showed that untreated 2VO group produced impaired tasks in MWM. Animals from 2VO group had the longest escape latency time, distance travelled and the least time spent in target zone in spatial memory and hippocampus dependent tasks of MWM. However, honey treated 2VO rats effectively improved the MWM performance in compared to untreated 2VO rats. However, there were no differences among honey treated group and Sham control on performing MWM tasks. This study revealed that tualang honey attenuated the cognitive deficits due to chronic cerebral hypoperfusion. Tualang honey provokes the neuroprotective effect with therapeutic prospects in AD. Our results suggest that tualang honey might be useful in the treatment of neurodegeneration related to cerebral hypoperfusion such as AD.

Keywords: tualang honey, neurodegeneration, neuroprotective, chronic cerebral hypoperfusion, Alzheimer's disease

POS003

Trans-resveratrol Lowers IOP by Smad Signalling Pathway

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Elevated intraocular pressure (IOP) in glaucoma is due to imbalance in extracellular matrix (ECM) homeostasis, which involves Transforming Growth Factor- β 2 (TGF- β 2). Trans-resveratrol (TR) has been shown to reduce IOP, although its mechanism of action is unknown. Objective: To elucidate involvement of TGF- β 2, SMAD signalling pathway and tissue and urokinase plasminogen activators (tPA and uPA) as the mechanism of TR-induced oculohypotension. Method: Confluent primary human trabecular meshwork cells (HTMC) were incubated with vehicle (Group 1); TR (25 μ M) (Group 2); TGF- β 2 (10 ng/ml) (Group 3); TGF- β 2 plus TR (Group 4). After 48 hours, cells were harvested to determine mRNA expression of TGF- β RI and II and SMADs 2, 3, 4, 6, and 7 using qPCR. Media were collected for estimation of tPA and uPA using ELISA. Results: Mean uPA concentration in the culture media was significantly reduced in Group 3 compared to Group 1. TR treatment in Group 2 and Group 4 increased the uPA concentrations by 1.5- and 1.4-fold, respectively, compared to Group 3. Mean tPA concentration in group 3 was 2.1- and 2.4-fold lower than Group 1 and Group 2, respectively. tPA was also significantly reduced in Group 4 compared to groups 1 and 2. The expression of TGF- β RI among the groups 2, 3 and 4 was significantly lower than the vehicle-treated group. Gene expressions for SMAD2 and SMAD3 were significantly downregulated in Group 3 and Group 4 compared to those in Group 1 and Group 2. The expression of SMAD7 in Group 3 was significantly downregulated but in Group 4 it was upregulated by 1.4-fold against Group 1 and Group 3. Conclusion: TR downregulates expression of TGF- β RI and upregulates SMAD7 hence, inhibits TGF- β 2 signalling in HTMC. This is also associated with elevated uPA secretion by HTMC.

Keywords: Trans-resveratrol; IOP; TGF- β 2; SMAD; glaucoma

POS004

Optimization of Time-point and Ratio of Human Osteoblast-osteoclast Co-culture System

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A small scale investigation was carried out, utilizing human bone cells of the osteoblast cell line (OB) hFOB 1.19 and osteoclasts (OC) extracted from peripheral blood mononuclear cells (PBMCs) in order to optimize the most appropriate time-point and ratio for co-culture system. The time-point optimization was performed within a week (Day 1, 3, 5 and 7) using Van Gieson Staining to detect the presence of collagen and Alizarin Red Staining for calcium. Optimization of co-culture ratio was carried out by applying the ratio of 1OC: 1OB, 1OC: 4OB, 2OC: 1OB and 1OC: 2OB respectively. Tartrate-resistant acid phosphatase (TRAP) Staining was used to detect the presence of TRAP activity as it is regarded as the histochemical marker for osteoclast activity. We have shown that collagen was successfully detected to be present at Day 1 whereas calcium was detected as early as Day 3. This implies that, the co-culture can be performed on Day 3 when the collagen and calcium co-exist as it indicates osteoblasts are building up bone tissue. As for the optimization of co-culture ratio, it was observed based on the results of TRAP staining that, 1OC: 2OB is the most appropriate ratio. Both of the bone cells were well-grown and dynamically balance up each other best as compared to the other three ratios. It can be concluded that, the optimization process is vital as it ensures the exact time-point and ratio of cells co-culture in order to produce a reliable and reproducible osteoblast/osteoclast co-culture system.

Keywords: PBMCs, osteoblast, osteoclast, co-culture, TRAP

POS005

The Cost Savings of Newer Oral Anticoagulants for Stroke Prevention in Patients with Atrial Fibrillation

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Strokes secondary to atrial fibrillation (AF) are estimated to incur higher direct costs due to severe disease with prolonged hospitalisation compared to non-AF strokes. Newer oral anticoagulants (NOACs) are considered as better alternatives compared to warfarin for stroke prevention in AF in terms of clinical effectiveness although the drug acquisition cost is more substantial. This study aimed to determine the direct stroke costs based on inpatient hospitalisation in a subgroup of National Health Service (NHS) Grampian, Scotland stroke patients, to evaluate the differences in costs related to AF stroke, and to ascertain if the use of NOACs within this study population would produce greater cost savings. Methods: Hospitalisation records over 5 years involving 3601 stroke patients were analysed. Direct inpatient costs were calculated based on the length of stay at different wards. The estimation of potential cost savings if AF patients had been on NOACs instead of warfarin were based on a cost simulation using efficacy data from a landmark clinical trial involving rivaroxaban, the ROCKET AF trial. Out of the total stroke cases, 29.5% of total stroke cases were secondary to AF, and associated with more severe and longer hospitalisations. Only 254 patients (39.4%) with confirmed AF were anticoagulated with warfarin prior to admission. AF patients incurred higher median costs (£4,719 [interquartile range, IQR £1,815 - £12,452]) compared to non AF patients (£3,267 [IQR £1,175 - £11,368]), although the association was statistically insignificant. The use of NOACs in AF-related patients with ischaemic strokes would potentially prevent more strokes (leading to 58 fewer cases in comparison to warfarin), resulting in a 17.1% in total cost reduction. AF stroke patients incurred higher total direct costs compared to non-AF cases. However, more cost savings were evident with NOACs, due to more strokes being prevented compared to warfarin.

Keywords: novel oral anticoagulants; cost saving; atrial fibrillation; stroke

POS006

The Central Vascular Markers among Young Women with Cardiovascular Disease (CVD) Risk Factors and Their Associations with Long Term CVD Risk

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Carotid intima media thickness (CIMT), pulse wave velocity (PWV) and augmentation index (AI) are central vascular markers which indicate vascular damage especially among patients with cardiovascular disease risk factors. The objectives of this study are to determine the associations among the three markers and their associations with long term CVD risk (30-year full CVD risk) in young women. One hundred and forty eight subjects were involved. They were healthy or may have CVD risk factors such as dyslipidemia, hypertension, and abdominal obesity or had family history of premature CVD. CIMT was measured by using ultrasound on the carotid artery walls while PWV and AI were measured via Vicorder. 30-year full CVD risk was calculated by using formula that incorporates the sex, age, smoker status, total cholesterol (TC), high density lipoprotein (HDL), systolic blood pressure (SBP), the use of antihypertensive medication and the presence of diabetes mellitus (DM). Data were analyzed via SPSS version 16. The mean age of the subjects was 29.97 ± 5.27 years old and the 30-year full CVD risk was $6.51 \pm 4.59\%$. There were no correlations between PWV and AI ($r = -0.11$, $P > 0.05$), AI and CIMT ($r = -0.03$, $P > 0.05$) and PWV and CIMT ($r = 0.07$, $P > 0.05$) after adjustment for the age. CIMT, PWV and AI were all significantly associated with future CVD risk, with AI having the strongest association ($r = 0.31$, $r = 0.35$ and $r = 0.38$ respectively). No linear associations among the three markers indicate that they may have different properties of vascular markers, whereby AI and PWV represents vascular function while CIMT represents vascular structure. Among all the markers, AI maybe can be used to classify future CVD risks among young women.

Keywords: arterial stiffness, cardiovascular, women

POS007

Potential of Vitamin E Isomers on Human Osteoblast hFOB 1.19 Cells: A Preliminary Study

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Several in vivo studies have shown that supplementation with vitamin E can improve bone structural and bone mechanical properties in animal models of osteoporosis. In this study we aimed to assess the cell viability and proliferative effect of Tocotrienol isomers in human osteoblast, hFOB1.19. Human Osteoblast hFOB1.19) was purchased from ATCC. Cells were seeded in 96 well culture plates at a density of 1x10³ per well and incubated overnight in growth media, DMEM F12 and 10% fetal bovine serum. After 24 hours, the cells were cultured in osteoblastic differentiation media (growth media +3mM Sodium Phosphate + 50Âµg/mL Ascorbic Acid). Cells were exposed to individual tocotrienol isomers ($\hat{1}^{\pm}$, $\hat{1}^2$, $\hat{1}^{\prime}$, $\hat{1}^3$ - tocotrienol) at various concentrations (1nM - 1000nM). The control group was treated with Osteoblastic Diffential Media only. Cell viability was assessed using 3-(4, 5-dimethylthiazol-2-yl)-5-(3-carbocymethoxyphenyl) 2-(4-sulfophenyl)-2H-tetrazolium (MTS) assay and analysed by microtiter plate reader at 490 nm. The percentage of viability hFOB1.19 cells was significantly increased at lower doses (1nM - 1000nM) as compared to the control group. $\hat{1}^{\prime}$ - and $\hat{1}^3$ -tocotrienol showed significantly increased of viability cells. Vitamin E isomers have the potential of enhancing cell viability and proliferation of hFOB1.19 cells in a concentration dependent manner.

Keywords: Osteoblast, Tocotrienol isomers, Viability

POS008

Inhibition of Chikungunya Virus Replication by Hesperetin and Naringenin

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Chikungunya virus (CHIKV) is an emerging arbovirus, which has recently become globally important. It poses a progressive major impact on humankind in recent years, with possibly life-threatening and incapacitating arthritis. Currently, there is no available effective antiviral drug for chikungunya infection. Thus finding and developing of lead compounds with anti-CHIKV activity that could be further developed to a practical treatment is urgently required. Several studies have reported the wide-ranging antiviral activities of flavanones; however, an inhibitory effect of selected compounds yet to be shown against CHIKV. In this study, we investigated the antiviral properties of two types of flavanones namely, naringenin and hesperetin against CHIKV in vitro replication. Our data have shown dose dependent inhibitory effects for naringenin and hesperetin against CHIKV intracellular replication using different assays including, CHIKV replicon cell line, time of addition and virus yield assay. Antiviral activity of the compounds was further investigated by evaluation of CHIKV protein expression using quantitative immunofluorescence assay and western blotting. Briefly, these compounds presented significant antiviral activity against CHIKV, reducing both CHIKV replication efficiency and down-regulating production of viral proteins involved in replication. Naringenin with $IC_{50}=6.818 \mu M$ ($SI=80.27$) and hesperetin with $IC_{50}=8.500 \mu M$ ($SI=23.34$) inhibited the post entry stages of CHIKV replication activity. In conclusion, obtained data from the current study suggest that naringenin and hesperetin could be potential candidates to be developed further as anti-CHIKV therapeutic agents.

Keywords: CHIKV, Flavanaone, infection

POS009

Annatto-derived Tocotrienol Promotes Cell Differentiation on Murine Preosteoblast MC3T3-E1 Cells

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Annatto-derived tocotrienol (AnTT) contains 90% δ -tocotrienol and 10% γ -tocotrienol, and has been shown to improve bone formation in animal models of osteoporosis. In this study, we aimed to elucidate the morphological changes during differentiation and activity of an early marker, alkaline phosphatase (ALP) on preosteoblast cells treated with AnTT. MC3T3-E1 cells were plated (1×10^4 cells/mL) in growth media (α -MEM + 10% serum) and incubated overnight. At initial day of investigation, the cells were cultured in differentiation media (DM; growth media + 3 mM sodium phosphate + 50 μ g/mL ascorbic acid) and treated with four concentrations of AnTT (0.001 – 1 μ g/mL). Ethanol was diluted in DM and used as vehicle. For cell morphology, cells were treated for 3, 6, 9, 15 and 21 days. After each time-point, morphology of the cells was visualized using inverted microscope Cell Imaging System (EVOS). For ALP activity, cells were treated for 1, 5 and 15 days. Cell lysates at all time-points were measured spectrophotometrically using p-nitrophenylphosphate as the substrate. The media for all the treatment groups were changed every 2-3 days. Results: Preosteoblasts were characterized by their spindle-shaped appearance. After 3 days, the cells changed morphology into cuboidal shaped. The cells reached sub-confluent cell monolayer with the long cells lying next to each other at day 6. After day 6, a whitish layer appeared on the cells. This layer is presumably the osteoid, i.e. the unmineralized portion of bone matrix that forms prior to the maturation of bone tissue. The osteoid appeared more abundant in AnTT-treated cells compared to the vehicle-treated cells. ALP activity was significantly higher in the 0.1 μ g/mL AnTT group ($p < 0.05$) compared to the vehicle at day 15 of treatment. In conclusion, annatto tocotrienol promotes differentiation of preosteoblast cells which was evident in the morphological changes and increased ALP activity.

Keywords: bone, osteoblast, osteoid, osteoporosis, vitamin E

POS010

Neuroprotective Mechanism of Propolis in Kainic Acid Induced Excitotoxicity in Rat Brain

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To understand the neuro-protective mechanisms of propolis, the activities of nitric oxide synthase (NOS), glutamine synthetase (GS), caspase-3 and nitric oxide (NO), thiobarbituric acid reactive substances (TBARS), total antioxidant status (TAS) and tumor necrosis factor- α (TNF- α) levels were studied in cerebral cortex, cerebellum and brain stem in rats injected with kainic acid (KA) and in rats supplemented with propolis prior to KA administration. Male *Sprague-Dawley* rats were divided into control group, KA group, propolis group and propolis + KA group with six rats in each group. Propolis group and KA + propolis group were orally administered with propolis (150mg/kg body weight), five times every 12 hours. Control group received vehicle. KA group and KA+ propolis group were given subcutaneous injection of KA (15mg/kg body weight) and were sacrificed after 2 hrs along with other groups. The brain regions were separated, homogenized and used for estimation of TBARS, TAS and GS by spectrophotometrically and NO, NOS, TNF- α , caspase-3 by commercial kits. Results were analyzed by one-way ANOVA and reported as mean $\pm$ standard deviation and $p < 0.05$ considered statistically significant. The concentration of NO, TBARS, TNF- α , activities of NOS and caspase-3 were increased significantly ($p < 0.001$) in all the three brain regions tested in KA group compared to the control. Propolis supplementation significantly ($p < 0.001$) prevented the increase in NOS, NO, TNF- α and caspase-3 due to KA. The concentration of TAS and GS activity was decreased ($p < 0.001$) in KA treated group compared to control group. Supplementation of propolis restored the concentration of TAS and GS activity decrease due to KA. Conclusion: Results of these studies clearly demonstrated that the propolis supplementation reduced oxidative stress, prevented the increase of NO, modulation of GS, inflammatory marker TNF- α and apoptotic marker caspase-3. Hence propolis may be acting through multiple targets to provide neuroprotection.

Keywords: Propolis, Kainic acid, Excitotoxicity, Neuroprotection, Rat brain

POS011

Behavioural Changes and Oxidative Stress in Kainic Acid-induced Neurodegeneration in Sprague-dawley Rats: The Protective Effects of Tualang Honey

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This study evaluated the potential protective effect of Tualang Honey (TH) against KA-induced behavioural changes, oxidative stress and neurodegeneration in rat cerebral cortex 48 hours after KA administration. Male Sprague-Dawley rats were divided into Control (saline), KA-treated, TH + KA-treated, Aspirin (ASP: anti-inflammatory agent) + KA-treated and Topiramate (TPM: antiepileptic agent) + KA-treated groups (n=6/group). Control and KA-treated groups were administered orally with drinking water, whereas TH + KA-treated, ASP + KA-treated and TPM + KA-treated groups were orally administered with TH (1.0g/kg BW), ASP (7.5mg/kg BW) and TPM (40mg/kg BW), respectively, five times at 12 hours intervals. KA (15mg/kg BW) was injected subcutaneously 30 min after last treatment to all groups except the control. Behavioural changes were observed using an open field test (OFT). Animals were then sacrificed after 48 hours of KA administration and cerebral cortex was collected for biochemical and histological assessments. All KA-treated groups had a status epilepticus. KA-treated group showed an increase in locomotor activity and hyperactive in the OFT which was attenuated by TH pre-treatment. Meanwhile, oxidative stress markers such as thiobarbituric acid reactive substances (TBARS) levels were elevated whereas, total antioxidant status (TAS) levels was decreased in KA-treated groups. TH pre-treatment significantly attenuated an increase in TBARS level and a decrease in TAS level. Histological analysis using Fluoro Jade C stain showed evidences of degenerated neurons in the piriform cortex of KA-treated groups at 48 hours after KA administration, which was not the case in the control. In contrast, the TH pre-treatment showed significantly reduced KA-induced neurodegeneration. The present study suggests that TH attenuates the KA-induced behavioural changes, oxidative stress and subsequently reduce neurodegeneration in the rat cerebral

Keywords: Tualang Honey, Kainic Acid, Neurodegeneration, oxidative stress, Sprague-Dawley rats

POS012

Histopathological Changes in Idiopathic Cutaneous Hyperchromia at the Orbital Region

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Dark circles around the eyes or idiopathic cutaneous hyperchromia at the orbital region (ICHOR) could be contributed by hyperpigmentation, hypervascularity or shadowing effect of tear trough. Dark eye circles is a major cosmetic problem, and is notoriously resistant to treatment. The key to a successful treatment is determining the primary cause, complying with maintenance and preventive regimens. This study aims to evaluate the histology changes in ICHOR skin, and also to correlate the clinical evaluation to histology analysis. This study is approved by Medical Research & Ethics Committee (NMRR-13-1267-16770). Forty nine (N=49) healthy volunteers requested for blepharoplasty had been recruited into the study. Plastic surgeons evaluated the periorbital areas and classified them into (i) hyperpigmentation (ii) hypervascularity or (iii) tear trough groups. The excised eyelid skin following blepharoplasty were collected and kept in 10% formalin for histology analysis. Paraffin-embedded tissues were processed for the Fontana-Masson silver stain for melanin deposition and distribution evaluation, or Pear's stain for evaluation of hemosiderin deposit. Data were analysed with SPSS software version 18.0. Categorical data were expressed as proportion and analysed via chi-square test. A total of 53.1% subjects was classified into hyperpigmentation group, 30.6% into tear trough and 16.3% into hypervascularity. Pearson chi-square test showed that hyperpigmentation group associated with high level of melanin deposit ($p<0.05$), and invagination of melanin into the dermal layer ($p<0.05$). Hypervascularity and tear through groups were associated with blood vessel dilatation ($p<0.05$). Presence of hemosiderin was not associated with ICHOR classification. Epidermal and dermal hyperpigmentation were the most predominant histological changes in clinically classified hyperpigmentation group. Therapy targeting on blood vessel dilatation might be useful in treating ICHOR associated with hypervascularity and tear through. This information is helpful in selecting the most effective treatment based on individual characteristics of the patient.

Keywords: dark eye circles, periorbital hyperpigmentation, Idiopathic Cutaneous Hyperchromia at the Orbital Re

POS013

Metabolomic Analysis of Female Reproductive System in Aging Mice: A Systemic Review

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Aging is known to impair human fertility. Recently, there has been an emerging interest regarding the application of metabolomics in understanding metabolites interaction with reproductive system that is related to infertility. Our objective of this systematic review is to assess the evidence-based literature in finding the most significant metabolites affected in reproductive aging. A scientific search was conducted in Google Scholar, Pubmed, Web of Science and SCOPUS for related studies. All articles between 2011 to 2016 and satisfied the inclusion criteria is considered for this review. Initial search found 11 relevant articles and it is revealed that only 3 articles matched the inclusion criteria. The studies showed that there are a few metabolites that are involved in female reproductive system due to aging. Previous research proposed that metabolomics analysis can identify some metabolites involving female reproductive system that may be affected due to aging. Thus, those findings can help to determine the related mechanisms involve in the long-term physiological changes associated with female reproductive system, fertility and aging.

POS014

In Silico Study on Anti-chikungunya Virus Activity of Hesperetin

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The re-emerging, *Aedes* spp. transmitted Chikungunya virus (CHIKV) has recently caused large outbreaks globally including countries in Europe and America. Promising inhibitory effects were observed in our previous in vitro study of hesperetin against CHIKV. In this study, we aim to identify possible target proteins for future underlying mechanistic studies using computational approach. 3-dimensional structures of CHIKV nsP2 and nsP3 were retrieved from the Protein Data Bank (PDB), whereas nsP1, nsP4 and the cellular factor sphingosine kinase 2 (SPK2) were designed using the Iterative Threading Assembly Refinement (I-TASSER) server based on respective amino acids sequence. We performed molecular docking on hesperetin against all four CHIKV non-structural proteins and SPK2 at parameters sufficient to cover the entire proteins. Proteins preparation and subsequent analysis of the different binding conformations of each protein were performed using appropriate software. The Lipinski's values of the ligand were computed and compared with the available data from PubChem. Interactions were observed between hesperetin and all five protein structures in this study, namely hydrogen bonds, pi-pi effects, pi-cation bonding as well as pi-sigma interactions with varying binding energies. Among all five tested proteins, our compound has the highest binding affinity with CHIKV nsP3 (3GPG) at -8.5 kcal/mol followed by nsP4 and SPK2 both at -7.7 kcal/mol, nsP1 at -7.6 kcal/mol and finally nsP2 (3TRK) at -6.9 kcal/mol. The designed ligand also matches the Lipinski's rule of five in addition to exhibiting closely similar properties with that of in PubChem. Hesperetin possesses interactions with all four CHIKV non-structural proteins in addition to SPK2 which plays a role in the virus replication cycle. These findings enhance our understandings on the possible underlying inhibitory mechanism of CHIKV replication, hence allowing further studies on these target proteins for the development of novel anti-CHIKV drug.

Keywords: In silico, computational approach, Chikungunya, antiviral, molecular docking

POS015

Computational Approach towards Exploring Potential Anti-chikungunya Activity of Selected Flavonoids

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Chikungunya virus (CHIKV) is a mosquito-borne alphavirus that causes chikungunya infection in humans. Despite the widespread distribution of CHIKV, no antiviral medication or vaccine is available against this virus. Therefore, it is crucial to find an effective compound to combat CHIKV. We aimed to predict the possible interactions between non-structural protein 3 (nsP) of CHIKV as one of the most important viral elements in CHIKV intracellular replication and 3 potential flavonoids using a computational approach. The 3-dimensional structure of nsP3 was retrieved from the Protein Data Bank, prepared and, using AutoDock Vina, docked with baicalin, naringenin and quercetagenin as ligands. The first-rated ligand with the strongest binding affinity towards the targeted protein was determined based on the minimum binding energy. Further analysis was conducted to identify both the active site of the protein that reacts with the tested ligands and all of the existing intermolecular bonds. Compared to the other ligands, baicalin was identified as the most potential inhibitor of viral activity by showing the best binding affinity (−9.8 kcal/mol). Baicalin can be considered a good candidate for further evaluation as a potentially efficient antiviral against CHIKV.

Keywords: Chikungunya, nsP3, flavonoids

POS016

Comparing Promethazine with Metoclopramide for Hyperemesis Gravidarum

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To compare the effects of promethazine with those of metoclopramide for hyperemesis gravidarum. Women at their first hospitalization for hyperemesis gravidarum were approached when intravenous antiemetic therapy was needed. They were randomly assigned to receive 25 mg promethazine or 10 mg metoclopramide every 8 hours for 24 hours in a double-blind study. Primary outcomes were vomiting episodes by diary and well-being visual numerical rating scale score (10-point scale) in the 24-hour main study period. Participants also filled out an adverse-effects questionnaire at 24 hours and a nausea visual numerical rating scale score at recruitment and at 8, 16, and 24 hours. A total of 73 and 76 women, randomized to metoclopramide and promethazine, respectively, were analyzed. Median vomiting episodes were one (range 0–26) compared with two (range 0–26) ($P_{.81}$), and well-being visual numerical rating scale scores were 8 (range 1–10) compared with 7 (range 2–10) ($P_{.24}$) for metoclopramide and promethazine, respectively. Repeat-measures analysis of variance of the nausea visual numerical rating scale scores showed no significant difference between study drugs (F score_0.842, $P_{.47}$). Reported drowsiness (58.6% compared with 83.6%, $P_{.001}$, number needed to treat to benefit [NNTb] 5), dizziness (34.3% compared with 71.2%, $P_{<.001}$, NNTb 3), dystonia (5.7% compared with 19.2%, $P_{.02}$, NNTb 8), and therapy curtailment owing to adverse events (0 of 73 [0%] compared with 7 of 76 [9.2%], $P_{.014}$) were encountered less frequently with metoclopramide. Promethazine and metoclopramide have similar therapeutic effects in patients who are hospitalized for hyperemesis gravidarum. The adverse effects profile was better with metoclopramide.

Keywords: Promethazine, metoclopramide and hyperemesis gravidarum.

POS017

Significant Activation of Systemic Interleukin-33 (IL-33) during the Late Critical Phase of Malaria Infection in Mice

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Malaria remains as one of the leading parasitic disease with high morbidity and mortality rate in the tropical and subtropical regions of the world. It is commonly associated with the activation and release of various inflammatory mediators, such as IL-1, IL-6, IL-18, TNF- α and IFN- γ leading to severe immunopathological reactions that commonly ended up with death. In this study, we proposed to investigate the involvement of Interleukin-33 (IL-33), a newly identified cytokine with both pro- and anti-inflammatory activities, during malaria infection. *Plasmodium berghei* ANKA infection in ICR mice was employed as model of malaria. Mice were inoculated with 2×10^7 parasitized red blood cells (PRBC) to initiate the infection. Parasitaemia was measured throughout the course of infection. Blood samples for determining the systemic concentration of IL-33 in the plasma were collected on day 1, 3 and 5 post inoculation. IL-33 concentration was measured by means of ELISA method. Malaria infected mice demonstrated a high degree of parasitaemia level followed by high mortality rate within 5-7 days after inoculation. Meanwhile, the systemic IL-33 level was found to be significantly elevated during the late phase of infection on day 5. A significant positive correlation between the elevated levels of plasma IL-33 and parasitaemia development was also observed. Results indicate the involvement of IL-33 during malaria infection and the positive correlation with parasitaemia development could well suggest that IL-33 may play an important role in mediating the severity of the infection.

Keywords: IL-33, Cytokine, Inflammation, Malaria, Immunology

POS018

Effects of Selected Coumarins on Plasma Membrane of Plasmodium Infected and Uninfected Red Blood Cells

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Coumarins are natural phytochemicals with diverse pharmacological effects. In this study, we aimed at investigating the effect of five coumarin derivatives, namely; umbeliferon, esculetin, scopoletine & herniarin, on the integrity and physiological function of plasma membranes in both *Plasmodium falciparum* infected and uninfected red blood cells (RBCs). Their effects on RBCs morphology, integrity and osmotic fragility as well as the parasite induced new permeation pathways (NPPs) were evaluated. Merozoite invasion and SYBR-green-I based drug sensitivity assays were also carried out to assess the parasite survival inside the RBCs. Their antioxidant activity was measured using the conventional in vitro tests and anti-lipid peroxidation assay. The molecular characteristics were determined using Molispiration-simulation-software. Results showed that all of the coumarin derivatives have weak to moderate growth inhibitory effect against *plasmodium falciparum*. In contrary, they protect against oxidative stress induced RBCs damage. The RBCs fragility and the *plasmodium* induced NPPs were not affected. Overall results suggest that the derivatives action against *plasmodium* is not related to their effect against RBCs. Further studies are therefore recommended to explore their precise mechanism of action.

Keywords: Coumarins, Isobologram, *Plasmodium falciparum*, SYBR green-I.

POS019

***Plasmodium berghei* Pathogenicity in Chloroquine-treated and Untreated Malarial Mice**

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Malaria is a devastating and lethal infectious parasitic disease that causes multiple organs damage. Previously, *Plasmodium berghei* induced histopathological changes in mice model was studied extensively and attributed to the predominance of the immunopathological response during the infection. In this study, we aimed at investigating the histopathological changes during the fully effective and partially effective malaria treatment with chloroquine. Mice were divided into six groups (n=6 each); negative control (uninfected), positive control (malaria untreated) and malaria groups treated with either 1, 5, 10 or 20 mg/kg of chloroquine (i.p). Chloroquine treatment were given at a time point whereby the parasitemia was in the range of 20-30%. During the subsequent days, body weight, complete blood picture, parasitemia development and the parasite aptitude to recrudescence were monitored. The mice were left for 10 days when there was no recrudescence until the parasitemia levels reached around 60-70%. Organs were then collected from the animals for histopathological study. Results showed that a complete parasite eradication was obtained at 20 mg/kg. Meanwhile, recrudescence occurred at 5 & 10 mg/kg after 1 & 3 days respectively and no effect was observed at 1 mg/kg. The partial therapy significantly prolonged the survival of malarial mice but it induced histopathological changes stronger than that of the positive control and characterized by stronger inflammatory changes. Nevertheless, a prominent splenomegaly, persistent anemia, leukocytosis and reticulocytosis along with histopathological changes which is milder than that of the positive control were observed. Overall results suggest that the severity of malaria induced organs damage is higher after recrudescence as compared to that of positive control at the same parasitemia level. Furthermore, immune reaction induced histopathological changes may persist even after a complete parasite eradication.

Keywords: Malaria, chloroquine, *Plasmodium berghei*, histopathology, recrudescence

POS020

Characterization of Flavonoids and Phenolic Acids in Leaves of *Clinacanthus Nutans* Using UHPLC-esi-orbitrap-MS/MS.

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Clinacanthus nutans (CN) or locally known as Belalai Gajah, is a perennial herb that has traditional uses in healing snake bites and herpes infections. To date, a detail chemical analysis of the constituents in CN is still limited possibly due to a low natural abundance of bioactives components, complex matrices and presence of multiple isomers. Our study is aimed to characterize the polar components of CN using ultra high performance liquid chromatography coupled to a high resolution mass spectroscopy (HRMS). Flavonoids and phenolic acids were extracted from plant matrix using methanol and ethanol. A gradient separation was performed on a C18 column with solvents 0.1% formic acid (A) and 0.1% FA in acetonitrile (B). The gradient method was 5%B (0 min), 19%B (10 min) and 95%B (13 min). The compounds were detected by MS under electrospray ionization in negative mode. Full scan (m/z 100-1000) was used with resolution 70,000 followed by a data-dependent MS2 scan. The HRMS analysis indicated that CN leaves are rich source of flavone glycosides. The major peaks detected were the flavone C-glycosides (14 compounds) and flavone O-glycosides (3 compounds) derivatives. Minor components such as the hydrocinnamic acids, flavonol, isoflavone and a phenylethanoid glycoside were also detected. Molecular isomers i.e. lucenin, lutanarin and rutin having same m/z values were successfully distinguished by its product ions. Structural isomers i.e. vitexin and isovitexin were harder to be distinguished as they produced the same product ions in the collision cell. However, the exact identification was achieved by optimizing the gradient separation on LC and comparison with reference standards. This study report for the first time a detail identification of the major flavonoids and phenolic acids in CN leaves which may shed valuable information in assessment of its health promoting and biological activities.

Keywords: *Clinacanthus nutans*, flavonoids, phenolic acids, high resolution mass spectroscopy, orbitrap

POS021

Topical Application of Natural Products Improved Wound Healing in Diabetic Rats

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Diabetic foot ulcer is one of the major complications of diabetes mellitus and may result in amputation. Early detection and appropriate treatment of these ulcers may prevent up to 85 % of amputations. The aim of the study was to compare the effectiveness of different topical natural products; Olive Heal, olive oil and vitamin E on the wound healing in normal and diabetic rats. The study was carried out using 56 male Sprague-Dawley rats which were assigned randomly into 7 groups: group I (normal wounded untreated), group II (normal wounded treated with Olive Heal), group III (diabetic wounded untreated), group IV (diabetic wounded treated with Jelonet®), group V (diabetic wounded treated with Olive Heal), group VI (diabetic wounded treated with olive oil), and group VII (diabetic wounded treated with palm vitamin E). Four full thickness excisions were made at the back of each rat. Wound healing was evaluated by rate of wound closure and histological assessment on the tenth day after wounding. All treatments showed high rate of wound closure significantly ($p < 0.05$) compared to groups I and III. For histological assessment on re-epithelization, group VI showed higher score compared to groups I and III ($p < 0.05$). There were no significant different between groups ($p > 0.05$) on collagen deposition and neovascularization scores. However, all treatments showed high histological scores compared to group III. Topical treatment of the natural products improved wound healing process in normal and diabetic rats.

Keywords: wound healing, diabetes, Olive Heal, palm vitamin E, olive oil

POS022

Relationship of Brain Derived Neurotrophic Factor DNA Methylation with Psychopathologic Symptoms and Antipsychotics in Stable Schizophrenia

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Brain derived neurotrophic factor (BDNF) contributes to dopamine neurotransmission by supporting the survival and differentiation of the neurons. During epigenetic event, methylated BDNF gene may cause reduction of its expression thus contribute to the clinical presentation and treatment response in Schizophrenia. Additionally, there are several confounding factors that may cause DNA methylation which include drug medication. The objective of our study is to quantitatively measure the DNA methylation level of BDNF and assess its relationship with psychopathological symptoms and antipsychotics. A total of 180 Schizophrenia cases were recruited from Psychiatry Clinic, Hospital Tengku Ampuan Afzan, and Kuantan Pahang were studied. Total genomic DNA from subjects was subjected to MethyLight Taqman analysis for quantitative measurement of BDNF gene DNA methylation. The psychopathological symptoms were assessed using Positive and Negative Syndrome Scale (PANSS). The treatment variables were gathered through the review of the medical records. There were no correlation between the DNA methylation level of BDNF with subdomains of PANSS except for positive subdomain ($r=0.04$, $p=0.03$). There was significant difference of DNA methylation level of BDNF between the Risperidone treated group ($1.310 \pm 0.033\%$) and typical antipsychotic treated group ($1.288 \pm 0.043\%$) ($p=0.013$). The relationship between DNA methylation of BDNF with positive symptom might indicate BDNF DNA methylation role in the manifestation of Schizophrenia. Treatment with Risperidone increases DNA methylation of BDNF as compared to typical antipsychotics. Both of these conclusions require further evaluation.

Keywords: BDNF, Schizophrenia, DNA methylation, Antipsychotic drug, MethyLight Taqman

POS023

Functional Characterisation of Aporphine Enantiomers at Htr2 Receptors

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Selective blockade of serotonin HTR2 receptors is of significant interest because of its involvement in cardiovascular function and certain mental disorders such as schizophrenia and insomnia. Recently, we discovered that two naturally-occurring aporphines, roemerine and nuciferine, possess high binding affinity for the HTR2A receptor. In this study we have used the TGF- β shedding assay to evaluate the functional activity of their respective (R)- and (S)-enantiomers at HTR2A, HTR2B and HTR2C receptors. (R)-roemerine was found to exhibit antagonistic effects on the three HTR2 subtypes (IC₅₀ = 224, 1120, 316 nM, respectively) with 5- and 3.5-fold selectivity for the HTR2A and HTR2C subtypes over the HTR2B subtype. In contrast, (R)-nuciferine showed stronger antagonistic activity at the HTR2B subtype (IC₅₀ = 253 nM) with 7.5- and 3.7-fold selectivity over the other two subtypes. In general, the corresponding (S)-enantiomers showed weaker antagonistic activity compared to the (R)-enantiomers at the three HTR2 receptors. The results showed that both the substitution pattern in the A-ring of aporphines and their stereochemical configuration have marked effects on their HTR2 receptor activity and subtype selectivity.

Keywords: Aporphines, enantiomer, HTR2 receptors

POS024

Do Our Diabetic Patients Know Their Medications?

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The prevalence of diabetes in the country is projected to reach a staggering 21.6% by the year 2020. Better knowledge and understanding of diabetic medications usually is related to better compliance to treatment leading to better glycaemic control, lower morbidities and also less mortality rates. The objective of this study was to evaluate the level of knowledge, attitude and practice of diabetic medications among diabetics attending the Greentown Health Clinic, Ipoh. This was a cross-sectional study using convenient sampling. 200 diabetic patients were enrolled in the study. The volunteers were each given a 32-item questionnaire (not validated) adapted from various questionnaires that assessed their knowledge, attitude and practice related to diabetic medications. Subjects who were above 18 years old and had been diagnosed for at least one year and on stable doses of medications for six months were given the questionnaire. This study showed that 126 respondents (63%) had a good level of compliance to their medication. Unfortunately, only 23% (N=43) of them had a good level of knowledge and the majority (65%; N=130) had a fair level of knowledge. Our study was not able to show a statistically significant association between age, gender, ethnicity, education level and monthly income with the medication compliance score. The level of knowledge on diabetic medications among the diabetics attending the diabetic clinic in Greentown Health Clinic, Ipoh is generally fair and requires some interventions. Various modes of health education among the diabetics in Greentown Health Clinic, Ipoh should be implemented to address this issue.

Keywords: Diabetes, diabetic, medications, compliance, knowledge

POS025

Tocotrienols Limit Bone Loss Through Suppression Of Osteoclast Formation And Activity: An Evidence-based Review

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Vitamin E has been shown to exhibit protective effects on bone. This systematic review mainly concerned about the effects of vitamin E homologues, tocotrienols in preventing bone loss through osteoclast differentiation and activities. A systematic literature search was performed to identify and assess relevant studies about the effect of tocotrienols in modulating the differentiation and bone resorbing activity of osteoclasts. By using SCOPUS and PUBMED MEDLINE search engine, 22 relevant studies were gathered. Regardless of languages or dates published, only 11 studies met the inclusion criteria and were selected. There were eight in vivo studies, two in vitro studies and a combination of both included in this review. Histomorphometric analysis for in vivo studies demonstrated reduction in osteoclast number following supplementation with tocotrienols. This is supported by data suggesting that changes in level of serum RANKL and OPG. Meanwhile in vitro studies concretely demonstrated the inhibitory effect of tocotrienols on osteoclast differentiation and activity. All study collectively revealed that tocotrienols successfully prevented bone loss through inhibition of osteoclastogenesis and its resorption activity.

Keywords: osteoclast, tocotrienols, bone loss

POS026

Functional Characterization of Cytochrome P450 2c19 (Cyp2c19) Allelic Variants Cyp2c19*23, Cyp2c19*24 and Cyp2c19*25

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Cytochrome P450 (CYP) enzymes are versatile oxidative catalysts responsible for the metabolism of an ever-expanding array of drug and xenobiotics. As one of the human CYP isoforms, CYP2C19 plays a major role in metabolizing approximately 10 % of the marketed drugs despite constituting a low hepatic CYP content of 5 %. Variation in CYP2C19 level and activity can be attributed to genetic polymorphism, and may lead to unforeseen drug responses such as over-reaction, toxicity or lack of responses. Hence, functional characterization of allelic variants is crucial to define the importance of CYP2C19 polymorphism in humans. The aim of this study was to explore the functional consequences of CYP2C19*23, CYP2C19*24 and CYP2C19*25 on the enzyme catalytic activity. All these alleles possess amino acid substitutions in their primary sequences (G91R and I331V in CYP2C19*23; I331V and R335Q in CYP2C19*24; and I331V and F448L in CYP2C19*25). Site-directed mutagenesis was performed to introduce nucleotide change for generation of the three variants. A validated omeprazole 5-hydroxylation high-performance liquid chromatography assay was used to examine important kinetic parameters such as Michaelis-Menten constant (Km), maximum velocity (Vmax) and IC50 of the expressed CYP2C19 wild type and allelic variants. Results showed that CYP2C19 allelic variants exhibited significantly lower catalytic activity compared to the wild type. However, in the inhibition study of CYP2C19 activities, results from the assay indicated that CYP2C19*23 was more susceptible to all four inhibitor probes investigated, namely ketoconazole, fluoxetine, sertraline and loratadine. These data suggested that individuals with CYP2C19 allelic variants are expected to have lower metabolism of omeprazole compared to the wild type CYP2C19*23 allele showed higher susceptibility to inhibition by the probes investigated.

Keywords: CYP2C19, genetic polymorphism, omeprazole

POS027

Abo And Rh (D) Blood Group Screening Among Medical Students- A Study From A Medical College In Malaysia

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The distribution of ABO and Rh (D) blood groups is different among different populations of the world. The objective of this study is to find out the distribution pattern of ABO and Rh blood group among medical students. 214 (71 males & 143 females) medical students were included. Blood was collected by finger prick method and a drop of monoclonal anti-A, anti-B and anti " D was added to a drop of cell suspension prepared from finger prick blood on clean white tile and mixed well. Results of agglutination were recorded immediately. A questionnaire about their blood group and other relevant data was collected through google doc. Blood group O was the most common (41.6%) in our study group. And the frequencies of the blood groups B, A, AB were found in order as 28%, 23.4%, and 7% respectively. The frequency of Rh +ve (94.8%) was more among the medical students than the Rh -ve (5.2 %). Blood group B Rh positive was most prevalent among the Malay students but among the Chinese and Indian students the most prevalent blood group was O Rh positive. The study showed that blood group O and the Rh +ve were more common whereas the blood group B Rh -ve was not seen among any of the medical students. In both males and females the most frequently occurring ABO blood group was O, followed by B, A, and AB.

Keywords: ABO Blood Group, Rh factor, Medical Students, Malaysia

POS028

Supplementation of Tocotrienol in Aging Mice Upregulates the Expression of Anti-aging Sirt 1 Gene in Viable Ovary

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The biological function of ovaries declines with age. In order to ascertain that the expression of targeted genes is due to the effect of particular treatment, the viability of tissue of interest needs to be confirmed, as a reduction in tissue viability causes a downregulation of gene expression in certain tissues. This study aim was to determine the viability of ovarian tissues from aging mice supplemented with tocotrienol (TCT) to be used for anti-aging gene expression analysis. Six months old female mice, *Mus musculus* were supplemented with either tocopherol-stripped corn oil (vehicle control) or tocotrienol at the doses of 150 mg/kg body weight (BW) orally per day for 30 days. Young mice at the age of 6 weeks were used as negative control while aging mice at the age of 7 months were used as positive control. At the end of the TCT supplementation period, mice were sacrificed by cervical dislocation for ovaries collection. One part of the ovarian tissues from young, aging and aging mice supplemented with tocotrienol were harvested for H&E staining to examine the viability of the ovarian tissues. Total RNA was isolated from the other part of the ovaries for gene expression analysis using QuantiGene Plex 2.0 Assay kits. All ovarian tissues used in this study were viable thus confirmed as suitable tissues to be used for gene expression analysis. Differentially expressed genes were involved in aging process. Following TCT supplementation in aging mouse, genes upregulated was anti-aging gene, SIRT 1 while genes downregulated were CDKN2A and E2F1, genes that regulate the expression of SIRT 1 gene. Tocotrienol was able to upregulates the anti-aging SIRT1 gene in viable mice ovary. The viability of the ovary is pertinent to the expression of anti-aging gene in order to help in understanding the mechanisms underlying ovarian aging and age-associated infertility.

Keywords: Tocotrienol, Aging, SIRT1 gene, Ovary

POS029

Short-term stability study of acyclovir-loaded solid lipid nanoparticles

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Poor oral bioavailability of acyclovir has become one of the major drug delivery concerns globally. In order to improve current pharmacokinetic limitations of acyclovir, nanoparticulate system have been explored and exploited as its delivery vehicles. Nanoparticles offer many great advantages that include physicochemical stability and sustained-release properties. Stability test is one of the important measures of a successful development of nanocarrier and a pre-requisite for future clinical trials of a pharmaceutical product. In this study, we aimed to observe the physicochemical stability i.e size, zeta potential and polydispersity index of solid lipid nanoparticles suspensions loaded with acyclovir. Two different types of solid lipid were evaluated in this study; glyceryl dipalmitostearate (Biogapress Vegetal BM 297 ATO) and glyceryl dibehenate (Compritrol 888 ATO), with polysorbate 80 (Tween 80) acted as emulsifying agent. After preparation of the acyclovir-loaded solid lipid nanoparticles based on the optimized formulations, the nanoparticles were stored at 4, 25 and 40 °C for a period of three months. All solid lipid nanoparticles containing acyclovir prepared from glyceryl dibehenate stored at 4 °C were considered stable throughout three months of testing period as no significant difference of particle size and polydispersity index were observed. Excellent particle's stabilization was achieved could be due to presence of free emulsifier in the suspension that prevent particle collision during storage at low temperature.

Keywords: stability studies, physicochemical stability, short-term test

POS030

***Hibiscus sabdariffa* Linn. Extract protects against high fat diet-induced cardiac injury**

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Obesity is a principal causative factor in the development of cardiovascular diseases such as hypertension and heart failure, by promoting oxidative stress. A local natural product, *H. sabdariffa* L. (Roselle) is enriched with natural antioxidants and demonstrated high potential in alleviating hypertension, hyperlipidaemia and body weight gain. Nevertheless, its effect on hearts of obese animals is still not clearly known yet. Therefore, this study was aimed to determine the effect of Roselle aqueous extract on cardiac function and structure in obese rat hearts. Male Sprague-Dawley rats were randomly divided into three groups (n=6 each group), ie: control which was fed with normal standard diet (18% kcal of fat) and obese (OB) and OB+Roselle (OB+R) which were fed with high fat diet (HFD, 60% kcal of fat) for 12 weeks. Roselle was given orally (100 mg/kg) to rats in OB+R group after 8 weeks induction of obesity for 4 weeks with continued diet. After 12 weeks, all rats were sacrificed and their hearts were excised and used for cardiac performance, biochemical and histological studies. All data obtained was analysed by one way ANOVA (post-hoc Tukey) to determine differences between groups. The systolic blood pressure (SBP) of HFD rats increased significantly ($p<0.05$). Langendorff-perfused rat hearts from OB group of rats had significantly ($p<0.05$) lower LVDP as compared to the control group, suggesting impaired contractile function. Interestingly, Roselle supplementation was able to lower SBP and improved LVDP and its derivatives in Langendorff-perfused obese rat hearts. In addition, Roselle was effective in lowering HFD-induced oxidative stress in the heart, as shown by increased superoxide dismutase and glutathione. Histological staining with Sirius Red showed increased fibrosis area due to obesity induction, which was also prevented by Roselle treatment. In conclusion, Roselle supplementation was able to improve cardiac injury condition in a rat model of HFD-induced obesity.

Keywords: Roselle; high fat diet; cardiac injury

POS031

The Effect of Roselle (*Hibiscus Sabdariffa* Linn.) Polyphenol-rich Extract As A Cardioprotective Agent In Streptozotocin-induced Diabetic Rats

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H. sabdariffa polyphenolic extract (HPE) has gained attention for its antioxidant properties. Until date, no attempt has been made to study the action of HPE towards cardiac function in diabetic condition. Hence, the aim of this study was to determine the effect of HPE as a cardioprotective agent in streptozotocin (STZ) induced diabetic rats. 32 male Sprague-Dawley rats (300-350g) were used in this study. Diabetes was induced by a single intraperitoneal injection of freshly prepared STZ, at a dose of 55 mg/kg in 0.9% normal saline. After 3 days of STZ administration, diabetic rats with glucose level above 15mmol/L were selected for the study. Diabetic rats were orally fed with 100 mg/kg of HPE daily for 8 weeks. Metformin at a dose of 150mg/kg was given to another diabetic group as a positive control. After 8 weeks, blood pressure was measured by using tail-cuff blood pressure system. The hearts then were excised and immediately connected to the aortic cannula of a Langendorff apparatus. Changes in heart mechanical dynamics, for example left ventricle developed pressure (LVDP) and coronary flow (CF) were then measured. One-way ANOVA (post-hoc Tukey) was used for statistical analysis and $p < 0.05$ was considered as significant different. The results showed that diabetic rats treated with HPE able to lower blood glucose, systolic and diastolic blood pressure significantly ($p < 0.05$) as compared with diabetic rats alone. HPE was able to improve heart function in STZ-induced diabetic rats as evidenced by a significant ($p < 0.05$) increased in the LVDP and CF as compared to diabetic group only. These results indicate the ability of HPE to improve myocardial contractility and coronary blood flow in STZ-induced diabetic rats. Hence, these findings suggest that HPE has potential effects as the cardio-protective agent in diabetes condition.

Keywords: Streptozotocin, Diabetes mellitus, *H. sabdariffa*, cardioprotective, Langendorff

POS032

Association between Cardiovascular Biomarkers and Long Term Framingham Risk Score among Young Women with Cardiovascular Disease Risk Factors

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C - reactive protein (hs-CRP) is an inflammatory marker while Photophletismography Fitness Index (PPGF) is a new marker to assess arterial stiffness. Both are used to assess the cardiovascular disease (CVD) risk factor in the future. This study is to determine the association between both markers and with long term Framingham risk score (30-years full CVD risk) among young women with CVD risk factors. The study included 148 young women, aged 20-40 years old and categorized into healthy group (HG) n=71 or having CVD risk factors (RG) n=77. CVD risk factors are defined as having hypertension, abdominal obesity, dyslipidemia, family history of CVD and smoking. Measurements done were hs-CRP and PPGF. 30-years Full CVD risk (30FCVD) were calculated based on points on age, sex, total cholesterol, high density lipoprotein, smoking status, systolic blood pressure, diabetes mellitus status and antihypertensive treatment. Data were analyzed using SPSS version 20 with $p < 0.05$ as significant level. The mean of age, 30FCVD and PPGF for all the subjects were 29.97 ± 5.27 years, $6.51 \pm 4.59\%$ and $48.79 \pm 8.91\%$ respectively. The level of hs-CRP was $0.85(3.45)$ mg/L. There was no correlation between hs-CRP and PPGF ($r = -0.02$, $p > 0.05$). Both markers show significant correlation with 30FCVD and hs-CRP have stronger association ($r = 0.33$, $p < 0.01$), followed by PPGF ($r = -0.18$, $p < 0.05$). hs-CRP is a more sensitive marker as compared to PPGF in assessing the future CVD risk among young women. The absence association between both markers may be due to different properties in which hs-CRP represent vascular inflammation while PPGF represent arterial stiffness.

Keywords: CVD, C - reactive protein, Photophletismography Fitness Index, FRS, inflammatory marker

POS033

Tocotrienol Reverses The Adverse Impact Of Corticosterone-induced Oxidative Stress on the Fertilizing Capacity of Epididymal Sperm in Rats

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Excess corticosterone (CORT) increases the formation of reactive oxygen species. This leads to a state of oxidative stress (OS), resulting in lipid peroxidation, apoptosis and impaired steroidogenesis in Leydig cells. Tocotrienol, a potent, chain-breaking antioxidant inhibits lipid peroxidation and reduces oxidative damage. This study aims to assess the effects of tocotrienol-rich fraction (TRF) on the oxidative status of CORT-treated rats. Design and Epididymides of fertile male rats were surgically-separated at the testis-caput junction. Twenty-four hours post-surgery, the animals received the following treatment daily for seven consecutive days: Tocopherol-stripped corn oil (control), CORT 25 mg/kg s.c. (CORT), CORT 25 mg/kg s.c.+TRF 100 mg/kg orally (CORT+TRF100) or TRF 100 mg/kg orally (TRF100). On day 8, experimental rats were co-habited with cyclic proestrus females. Sperm-positive vaginal smear indicated pregnancy, and the females were left until term to assess pregnancy outcomes. Experimental males were then sacrificed, central blood collected immediately and the plasma obtained was later analysed for malondialdehyde, MDA (an end product of lipid peroxidation) concentration and antioxidant enzymes (glutathione peroxidase, GPx and superoxide dismutase, SOD) activities as biomarkers of oxidative damage. Plasma levels of MDA was increased ($p=0.002$), while GPx and SOD activities were decreased ($p=0.000$) in the CORT group compared to that of control, suggesting a state of CORT-induced oxidative stress. Conversely, administration of TRF to CORT-treated rats decreased MDA levels ($p=0.008$), and increased GPx and SOD activities ($p=0.001$ and $p=0.011$ respectively) in the CORT+TRF group compared to CORT group. Furthermore, the number of blastocyst implantation, live fetuses and fetal birth weight in females mated with CORT+TRF-treated males were significantly higher compared to that of CORT group. In conclusion, 100 mg/kg/day TRF supplementation reversed the OS-induced effects of exogenous CORT on the parameters studied and restored the fertilizing capacity of rat epididymal sperm, thus exhibiting a beneficial effect on the male reproductive potential.

Keywords: Corticosterone, tocotrienol, epididymal sperm

POS034

Effect of Derivatives of Neuroactive Amino Acids on Respiratory Functional Changes in the Cardiac Mitochondria of Stressed Animals.

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The stress reaction is characterized by damage of cells and tissues in several organs, particularly, in the heart. Cardiac mitochondrial dysfunction is considered to be one of pathogenetic mechanisms resulted from excessive release of catecholamines and glucocorticoids. Thus, there remains a need for novel cardioprotectors that can prevent damage of cardiac mitochondria. The purpose of this research was to investigate effect of neuroactive amino acids derivatives (γ -aminobutyric acid (GABA) and glutamate) on cardiac mitochondrial function of stressed animals. The experiments were done on 32 female rats. Stress reaction was induced by hanging animals at dorsal cervical skin position for 24 hours. Female rats were divided into 4 groups: control rats (groups 1), stressed rats received saline solution (group 2), stressed animals received glufimet (glutamic acid derivative) in dose of 29 mg/kg (group 3) and stressed animals received phenibute (GABA derivative) in dose of 50 mg/kg (group 4). The mitochondrial fraction was taken by differential centrifuging of heart homogenate. Respiration was measured by mitochondrial polarography using Clark electrode for measuring coupled respiration in freshly isolated mitochondria. The functional state of mitochondria was assessed using Respiratory Control Ratio (RCR), which was calculated as the ratio of the oxygen consumption rate in the presence of 0.2 mM ADP to the rate without ADP. Potassium malate (0.5 mmol)/potassium glutamate (0.5 mmol) and potassium succinate (1 mmol) were used as the substrates for first and second respiratory chain complexes. It was shown that stress induced by immobilization and pain leads to uncoupling of respiratory and oxidative phosphorylation processes in cardiac mitochondria that were expressed as reduction of RCR by 35.3% in presence of malate/glutamate and by 37.3% in presence of succinate. Both glufimet and phenibute significantly decreased the stress damaging effect on mitochondria. RCR of mitochondria in the group of rats receiving glufimet was 45.4% higher for malate/glutamate and 48.6% higher for succinate as to compare with stress control. For animals received phenibute, RCR was 34.1% higher in presence of substrate of the first respiratory complex and 51.3% higher when used substrate of the second respiratory complex. Thus, stress induced by immobilization and pain leads to uncoupling of respiratory with oxidative phosphorylation in cardiac mitochondria, while GABA and glutamic acid derivatives decrease mitochondrial damage in heart of stressed animals.

Keywords: Mitochondria, stress, derivatives of GABA and glutamate

POS035

Tocotrienol Rich Fraction (Trf) Supplementation Produces Higher Numbers of Normal 2-cell Embryos in C57bl/6 Mice

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Healthy preimplantation embryos are crucial in establishing a successful pregnancy. Good maternal nutrition in early development markedly contributes to the future health of embryos. Many studies have shown that Vitamin E exerts cellular antioxidant effects. Palm oil tocotrienol-rich fraction (TRF) consists of both tocopherol and tocotrienol isomers of vitamin E. It has been shown to significantly improve preimplantation development in outbred mice, but its effect on the morphological quality of early embryos has not been examined. The aim of this study is therefore to ascertain the effect of TRF supplementation on embryo quality at the 2-cell stage, in C57BL/6 mice. A total of 856 C57BL/6 mouse embryos were obtained from 57 females, aged 10-12 weeks. The female mice were divided into three treatment groups. Mice in each treatment group were given oral gavage of 60 mg/kg body weight per day of corn oil (control), palm TRF or alpha-tocopherol for 7 consecutive days. On Day-6 of treatment, mice in each group were superovulated with 5 IU of Pregnant Mare Serum Gonadotrophin (PMSG), followed by 5 IU of human chorionic Gonadotrophin (hCG) 48 hours later. They were then mated with fertile males, at a ratio of 1:1. At 46-48 hours post hCG, the females were euthanized. Two-cell embryos were then harvested and morphologically assessed as either normal or abnormal embryos. The embryos were classified based on the evaluation of the number of blastomeres and the degree of fragmentation. Normal 2-cell embryos were characterized as having evenly sized blastomeres, each containing one nucleus, with less than 10% fragmentation of the total cytoplasmic volume. The production of abnormal 2-cell embryos was found to be lowest in TRF (10.6 ± 7.3), followed by corn oil (20.8 ± 2.0) and alpha-tocopherol (18.8 ± 11.7). TRF supplementation produced significantly ($p < 0.05$) lower numbers of abnormal embryos compared to corn oil and alpha tocopherol supplementation groups. TRF maternal supplementation may be explored as an effective and safe means of producing better quality early preimplantation embryos, which may contribute to better fetal health and improved pregnancy outcomes.

Keywords: Tocotrienol-Rich Fraction (TRF), embryo morphology, mouse embryos, maternal supplementation

POS036

Phytochemical Analysis and Antimicrobial Activity of Methanolic Extract of *Phyllanthus niruri* (Dukung Anak)

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This study was conducted to investigate the phytochemical properties and antimicrobial activities of methanolic extract from various plant parts (leaf, stem and root) of *Phyllanthus niruri* (Dukung Anak). Preliminary phytochemical analysis for alkaloids, glycosides, carbohydrates, phenolic compounds, tannins, saponins, free amino acids, proteins, flavonoids, steroids and triterpenoids were made by following standard procedures. The in vitro antimicrobial activity was tested against several bacteria and fungi that most commonly infected human body: *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Bacillus cereus*, *Staphylococcus epidermidis* and *Candida albicans*. The preliminary phytochemical screening of *P. niruri* have revealed the presence of alkaloids, glycosides, phenolic compounds, tannins, saponins, flavonoids and steroids. The leaf part of methanolic extract was found to have higher chemical constituents than other vegetative parts. The root, stem and leaf methanolic extract showed inhibition zone against all gram positive bacteria tested while only root and leaf part showed activity against one gram negative bacteria tested (*K. pneumonia*). For fungus, no inhibition zone was observed. The widest inhibition zone was exhibited by stem part extracts against *S. aureus* (17.55 mm). This study suggested that the phytochemical constituents of *P. niruri* has broad spectrum antimicrobial potential that is effective in the management of microbial infections.

Keywords: *Phyllanthus niruri*, antimicrobial, phytochemical analysis, methanolic extracts

POS037

The Effect of Mild Hypothermia and Progesterone on Glutamate Toxicity in Primary Cortical Astrocytes

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Astrocytes are the most abundant brain cells that supply neurons with trophic support, modulate information processing and protect the neurons against damage. Therapeutic hypothermia has been proposed to exert neuroprotection in the ischemic brain cells. Progesterone is a neurosteroid that synthesized in neurons and astrocytes and is involved in repairing the brain cells after ischemic injury. The aim of this study is to investigate the effect of mild hypothermia and progesterone on the cell viability, the level of glutamate uptake and S100 β in the astrocytes. The culture of primary astrocytes was prepared from the cortex of postnatal rat pups. The ischemic injury was induced by exposing the astrocytes with excessive concentration of glutamate. After the exposure, the primary astrocytes were subjected to normothermia (37 $^{\circ}$ C) and mild hypothermia (33 $^{\circ}$ C) with 10 μ M of progesterone for 24 hours after glutamate toxicity. The viability of astrocytes was measured using MTT assay and the level of glutamate uptake and S100B were estimated using ELISA. A two-way ANOVA was conducted that examined the effect of the treatment group and condition treatment on primary cortical astrocytes cell. There was significantly increased in the number of viable astrocytes in the mild hypothermia-treated with progesterone (M = 87.67, SD = 12.53) when compared to normothermic astrocytes (M = 79.24, SD = 21.66). There was an increased in the glutamate uptake (F (3, 40) = 0.842, p>0.05) and significantly decreased in the S100B level (F (3, 8) = 2207.546, p<0.01) of mild hypothermia-treated with progesterone when compared to normothermic astrocytes. In conclusion, our observations suggest that combination of mild hypothermia and progesterone reduced the glutamate-induced injury by enhancing the glutamate uptake in the primary cultured rat astrocytes.

Keywords: Hypothermia, Progesterone, Neurosteroid, Glutamate, Astrocytes

POS038

Role of Thyroid Hormone in the Regulation of Uterine Fluid Environment and Development of Uterine Receptivity in Rats

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Successful embryo implantation requires precise regulation of the uterine fluid environment which is under the control of sex-steroids. Estrogen and progesterone have been shown to affect the uterine fluid parameters, such as volume, pH and electrolytes content through regulating the expression of membrane transporters in the endometrium. Several hormonal and environmental factors can interfere with this regulation, resulting failure of embryo implantation. We hypothesized that thyroid hormones play a role in regulation of uterine fluid via affecting expression and functional activity of several membrane transporters in the endometrium which are involved in fluid regulation. This hypothesis was based on the observation that the lack of thyroid hormone or hypothyroidism is associated with high failure rate of embryo implantation, contributing to infertility. In this study, female SD rat model was used to investigate these changes. We induced hypothyroidism in 34 female rats by 21 days treatment of 0.05% methimazole in drinking water daily during treatment. After treatment, plasma thyroxine (T4) level was measured by Rat thyroxine ELISA kit (Cusabio Biotech Co.). Plasma T4 levels of 34 female rats were found below the lowest level (20ng/ml) of ELISA kit provided standard. Then the hypothyroid female rats were given for mating with normal male SD rats at 2:1 ratio. Pregnancy was confirmed by the presence of sperm in vaginal smears of 24 female rats. The 24 rats were then divided into 4 groups (n=6) and received thyroxine through subcutaneous injection at different doses from one day after the gestational day. The thyroxine treatment was for four consecutive days. At the end of treatment (day 5), rats were sacrificed and uteri were collected for further investigations. This study is important to identify the role of thyroid hormone in the regulation of uterine fluid environment which is crucial for early pregnancy establishment.

Keywords: Hypothyroidism, Rat, Pregnancy, Thyroid hormone, Uterus

POS039

**Conditioned Media from Rat Amniotic Fluid Stem Cells Accelerates Wound Healing;
an In Vitro Study in Diabetic Human Dermal Fibroblast**

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Growing evidence has observed the presence of angiogenic growth factors available in conditioned medium (CM) prepared from stem cells. In the recent approach, we reported that CM prepared from Rat Amniotic Fluid Stem Cells (rAFSCs), contains high levels of angiogenic factors that significantly promoted wound healing. The CM was prepared from rAFSCs; where the appropriate number of stem cells required was predetermined. The production of CM from rAFSCs is in the presence of Leukaemia Inhibitory Factor (LIF+) and absence of LIF (LIF-). The pluripotency of the cells is verified with the level of OCT4 and NANOG. Enzyme Linked Immunosorbent Assay (ELISA) and Western blotting technique were used to identify and confirm the expression and presence of selected angiogenic markers in the developed rAFSCs-CM. To substantiate the efficacy of the CM, Scratch test assay was conducted to observe effective cell migration with the addition of CM. The angiogenesis factors, VEGF and TGF- β 1 were markedly upregulated in CM, when LIF was not present (CM LIF-) compared to that when LIF is present (CM LIF+). This results was substantiated with the observation made in Scratch Test Assay when CM LIF- significant accelerated wound closure compared to the cells when incubated with CM LIF+ of HDF-D in CM LIF-. This observation has suggested that potential development should be conducted for further development of CM to enhance wound healing.

Keywords: Rat amniotic fluid stem cells, conditioned medium, diabetic wound healing angiogenic factors, growth

POS040

Effects of Nicotine on the Cytoskeletal Structures of Pre-implantation Embryos in Mice

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Cytoskeleton is important structures for cell functions and embryo development. Damage to the cytoskeleton renders the affected cell non-viable and the cell will not completely develop and survive. However, report on the effects of nicotine on cytoskeletal structure is lacking. This study aimed to investigate the effects of nicotine on the cytoskeletal structures of pre-implantation embryos at 2- and 8-cell stages using a Confocal Laser Scanning Microscope (CLSM). Twelve female mice (5 weeks old, 15-16 g) were divided into two groups with six female in a group; group A received 0.9% NaCl (control) subcutaneously (s.c) while group B was injected with 3.0 mg/kg/day nicotine s.c (treated) for 7 consecutive days, respectively. Animals were then superovulated, cohabited overnight with fertile male and euthanized by cervical dislocation 24 h post coitum. Embryos at 2- and 8-cell stages were flushed and fixed with 4% paraformaldehyde for 24 h. Fixed embryos were stained with Alexa Fluor 594 Phalloidin and Anti-alpha Tubulin Antibody to visualize actin and tubulin distribution under the CLSM. Labelled embryos were scanned using CLSM and images were analysed with LAS AF Lite software. Results showed that the mean $\pm$ SEM fluorescence intensities of actin at 2-cell stage in the nicotine group were 22.3 ± 0.1 as compared to control group (saline) with value 22.0 ± 0.7 ($p>0.05$). At 8-cell stage, there were significant difference between the nicotine group vs saline (mean $\pm$ SEM intensities of actin = 9.2 ± 0.6 vs 28.1 ± 2.5 respectively, $p<0.001$). While in tubulin, there were significantly different in 2- and 8-cell stages for nicotine vs saline (mean $\pm$ SEM intensities of tubulin 2-; 8-cell stages = 13.7 ± 1.1 vs 25.2 ± 1.1 , $p<0.001$; 4.2 ± 0.7 vs 50.7 ± 3.7 , $p<0.001$, respectively). This study suggests that the effect of nicotine on the actin and tubulin of 2- and 8-cell stages of embryo may affect the development and survivability of the embryo.

Keywords: Actin, tubulin, nicotine, intensity, cell stage, pre-implantation embryo

POS041

Relationship between Lifestyle Factors and Bone Density among Female Pharmacy Students in UiTM

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Low bone mineral density (BMD) and osteoporosis are serious general health issues in Asia especially in postmenopausal women. Healthy lifestyle is known to improve this issue, however lifestyle behaviours and other factors influencing BMD is still controversial. Identifying the bone health status at younger age is essential in order to prevent osteoporosis in the future. Previous studies on BMD among young women in Malaysia are limited. This study aimed to determine that lifestyle factors influence BMD in young women. In a cross-sectional study, a total of 276 female Pharmacy students in UiTM were interviewed using questionnaires regarding their background and lifestyles. Calcaneal BMD was measured using ultrasound bone densitometry. Relationship between BMD and lifestyle factors were evaluated by SpearmanTM's correlation test. A Chi-square test was used to see any significant difference between BMD and lifestyle variables. All tests were two-tailed and a 5 percent level of statistical significance was chosen. Analysis showed that out of 276 female Pharmacy students, 62.0% were of normal BMD, 35.1% were osteopenia and 2.9% osteoporotic. BMD were correlated with body weight, height, body mass index (BMI), body fat and sunlight exposure while there was no correlation between BMD with exercise, physical activity, calcium supplement intake and caffeine intake.

Keywords: bone mineral density, osteoporosis, healthy lifestyle, bone densitometry

POS042

The Effect of Centella Asiatica Extract on Experimental Cognitive and Neuroplasticity

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Centella asiatica is one of the important medicinal and nutraceutical herbs being used by ethnic people since prehistoric times. Secondary metabolites obtained from the plants are found to be an important source of phytochemicals that could be used directly or as an intermediate for the production in pharmaceutical in foods and drink supplements. Limited success and potential complication of modern drugs also has led to large shift of people seeking for an alternative herbal medicine. Neuroplasticity or also known as cortical re-mapping is refers to brains ability to response as a result of a certain experience. Neurogenesis and neuroplasticity could be involved in the various temporal phases of human disorder and in several cognitive alterations. The proposed study was sought to determine the cognitive and neuroplasticity study towards memory enhancement. The rats were divided into five groups which are negative control, positive control, low dosage, medium dosage and high dosage that were supplemented with distilled water, 200mg/kg, 400 mg/kg and 800 mg/kg respectively for three weeks. The extracts were given orally by force-feeding. Stress also were induced for the positive control, low dosage, medium dosage and high dosage using force swim test and restrain method. After three weeks, behavioral study assessment which is Novel Object Discrimination (NOD) and Morris Water Maze was carried out. Performance of the rats was evaluated by the time of exploring familiar and novel object and also the discrimination index (D2) for the NOD, whilst for Morris Water Maze is the duration of time the rats reach the platform. Based on the results, the treatment groups show postive value of D2 and duration of time to reach the platform which medium and high dosage was significantly different to control group. Therefore, this study suggested that *Centella asiatica* enhanced memory and learning in rats.

Keywords: *Centella asiatica*, cognitive, neuroplasticity, neurogenesis, memory

POS043

Stress Induced Drinking- Alcohol: Friend Or Foe?

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Alcohol drinking has a strong association with stress and tension among people. Public has a perception that, alcohol drinking reduces tension, anxiety and stress level and the 'tension reduction hypothesis' was proposed previously. Literature documents conflicting report regarding the use and abuse of alcohol. Few studies supports the notion that 'ALCOHOL REDUCES STRESS'; on the other hand reports also confirm that 'ALCOHOL DRINKING ENHANCES THE STRESS'. Due to these conflicting results there is not yet a confirmatory report with respect to the drinking habits among the public. To evaluate the possible contributors of alcohol drinking habits among Sabahan population. Perceived stress leads to alcohol drinking among the public? Alcohol drinking further increases the stress? It is a cross sectional study. Ethical approval (JKETika 2/13(9), dated 28-10-2013) was received. Selection of participants was random with age between 18-50 years of either sex. Sample size was 220 out of which 121 samples were valid. A valid stress questionnaire (DASS 21) and alcohol audit questionnaire were used in the study. The study areas included selected areas Sembulan, Putatan, Inanam, Penampang and Kota Kinabalu city area. Validity of the questionnaires were tested by using Chronbach's alpha. Data was compiled and analysed by structural equation modelling using software SPSS AMOS version 23 (Suki 2015). $P < 0.05$ was considered as the level of significance. Results: Level of stress was the major factor that induced drinking. Stress led to drinking and drinking based on stress enhanced the stress level. In conclusion, stress led to alcohol drinking. Alcohol drinking due to stress aggravates stress. It is a vicious cycle. Alcohol drinking during stress aggravates the stress. Stress-Alcohol-Stress is a vicious cycle.

Keywords: stress perception, alcohol drinking

POS044

The Determination of Erythroxylum Cuneatum Leaves Extract Effects on Memory in a Novel Object Recognition Task in Rats

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Erythroxylum cuneatum (*E. cuneatum*) has been used traditionally in treating drug addiction and other illness. Drug addiction is commonly associated with impairment in cognitive performance. Due to its lack of information on neurobehavioural properties of the plant, this elusive plant was investigated further to delineate the effect of *E. cuneatum* on cognitive performance in rats. Working memory task using Novel Object Discrimination test (NOD) were performed for the determination of neurobehavioral profiles. 56 male Wistar rats were used in the study and divided into seven groups which a normal group, control group, two groups of positive drug control and three groups of three different doses of alkaloid extracts (5, 25 and 50 mg/kg). All doses were chronically administrated intraperitoneally to the test group for 21 consecutive days and evaluated on day 21 after the last dose. In the Novel Object Discrimination test, alkaloid treated rats did not show any significant discrimination between the familiar and novel object ($P > 0.05$) thus, it can be interpreted as not induce a memory deficit. It can also be postulated that the extract has no effect on memory and learning; neither improves nor impairs the cognitive function. In conclusion, since *E. cuneatum* does not show any impairment on cognitive, its pharmacological properties could be further investigated without significant changes in cognitive performance.

Keywords: Erythroxylum cuneatum, Chinta Mula, Novel Object Discrimination Test, Working Memory

POS045

Does Zerumbone Reverse House Dust Mite-Induced Airway Epithelial Barrier Dysfunction?

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Human lung epithelial barrier acts as the first line of defence in the airway system as the lining came into contact with allergen from the air breathe in during the respiration process. Disrupted airway epithelial barrier facilitates the recognition of allergen by immune cells and leads to inflammation of the airway lining of the respiratory system which may result in chronic condition such as asthma. Airway epithelial barrier may be disrupted by a common household allergen called house dust mites (HDM) which contains Der p 1, a cysteine protease that is capable to cleave the junctional proteins such as occludin and E-Cadherin. Zerumbone, an active compound derived from the rhizome of *Zingiber zerumbet*, has been reported to exhibit anti-allergic effect via modulation of Th1/Th2 cytokines in an asthmatic mouse model. As airway epithelial barrier plays a central role in the sensitisation to allergens and pathogenesis of allergic asthma, this study aims to investigate the protective effect of zerumbone on the HDM-induced airway epithelial barrier dysfunction. MTT assay was carried out to determine the cytotoxicity of zerumbone on Calu-3 cells, a human lung epithelial cell line used in this study. The protective effect of zerumbone against the proteolytic effect of HDM on the junctional proteins was investigated by studying the expression of junctional proteins by immunoblotting. The transepithelial electrical resistance (TEER) reading was recorded to measure the integrity of the epithelial barrier. Initial trial of immunoblotting showed that the protein expression of E-Cadherin and occludin was preserved in Calu-3 cells induced with HDM and treated with zerumbone for 24 hours. Initial trial of TEER also showed that zerumbone reversed the effect of HDM on the integrity of the airway epithelial barrier at 24 hours incubation time. Zerumbone may reverse the effect of HDM-induced airway epithelial barrier dysfunction. However, this finding requires further study as limited trials have been carried out.

Keywords: Epithelial, Asthma, House Dust Mite, Calu-3, Tight Junction

POS046

Effect of Quercetin on Oxidative Stress and Inflammation in the Heart of Diabetic Rats

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Quercetin is a bioflavonoid widely available in fruits and vegetables. This compound has been known to possess anti-oxidative and anti-inflammatory effects. We tested the hypothesis that quercetin can help to ameliorate heart damage in diabetes. Therefore this study aims to investigate the effect of this compound on parameters related to myocardial damage in diabetes which include oxidative stress and inflammation. Streptozotocin-nicotinamide induced male diabetic rats were given quercetin at 10, 25 and 50mg/kg/day for 28 consecutive days. Blood glucose level was weekly monitored and at the end of the treatment, rats were sacrificed by cervical dislocation and blood was again collected and analysed for fasting glucose (FBG), glycated haemoglobin (HbA1c) and lipid profile levels. Heart was harvested and either homogenized or subjected for histological studies. Homogenized heart tissue was subjected for analyses of protein activity and expression levels. Quercetin treatment to diabetic rats reduced FBG, HbA1c and lipid profile levels (except HDL) and decreases oxidative stress level (as featured by reduced MDA and increased anti-oxidative enzymes-SOD, CAT and GPx). Additionally, the level of inflammation as featured by interleukin and TNF- α levels decreased. Blood level of cardiac injury marker also decreased. Following quercetin treatment, lesser histopathological changes were observed in diabetic heart. Quercetin is a potential agent which can be used to ameliorate myocardial damage in diabetes and thus can be used in the treatment of diabetic cardiomyopathy.

Keywords: quercetin, cardiomyopathy, oxidative stress, inflammation

POS047

***In silico* Analysis and Reporter Gene Construct Generation of Karyopherin Alpha 2 Promoter**

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Introduction: Nuclear receptors are proteins found within the cell and work with other proteins to regulate the expression of specific genes responsible for controlling the development, homeostasis, and metabolism of the organism. Nuclear receptors possessing nuclear localisation signals enter the nucleus with the help of karyopherins. Karyopherins are nuclear import factors that interact with nuclear receptors or any other cargo proteins containing nuclear localisation signals and mediate their import into the nucleus. There are seven karyopherin alphas (KPNA) encoding genes and they show cargo specificity. To date, no experimental data are available to define the mechanism of transcriptional regulation karyopherin alpha genes especially in humans. **Objective:** To examine the association of nuclear receptor-dependent regulation of the human KPNA2 promoter using *in silico* analysis and the generation of its reporter gene construct. **Methodology:** *In silico* analysis was carried out to identify the promoter region of human KPNA2 and the nuclear receptor binding sites within the identified promoter. The NCBI gene database was employed to identify 20kb KPNA2 sequence for human, rat, mice, cattle and dog. Subsequently the 20kb sequence of the human KPNA2 gene was selected as the reference sequence and aligned against the equivalent region in rat, mice, cattle and dog using VISTA analysis. Upon identification of the proximal promoter position, MatInspector software was employed to determine putative nuclear receptor binding sites within the human KPNA2 promoter region. Upon completion of *in silico* analysis, generation of reporter gene construct was carried out by designing a specialised pair of primers containing Acc65 and HIND III restriction site within it, followed by running PCR using these primers to amplify the sequence of the human KPNA2 promoter region. The amplified region was then cloned into a reporter vector (pSEAP2-Basic) and the clone generated was validated through sequencing. **Results:** A 2.6kb human KPNA2 promoter region was identified and 155 nuclear receptor binding sites were detected within it using *in silico* analysis. In addition, the human KPNA2 reporter gene construct was successfully generated and the promoter sequence was validated by sequencing. **Conclusion:** The association of nuclear receptor and human KPNA2 promoter was validated by *in silico* analysis. Although, the reporter gene construct was successfully generated, the impact of nuclear receptor in regulation to the human KPNA2 expression warrants future investigation.

Keywords: nucleocytoplasmic shuttling, karyopherin $\alpha 2$ (KPNA2), nuclear receptor, *in silico* analysis, cloning.

POS048

Effects Of *Erythroxylum Cuneatum* Leaf Alkaloid Extract In Carrageenan-induced Inflammation in Sprague Dawley Rats

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Erythroxylum cuneatum is a tropical flowering plant found in the family Erythroxylaceae. It is used in Thai traditional medicine for anti-inflammatory and anti-pyretic purposes, but its medicinal value has a very limited report. The objective of the present study is to determine the antiinflammatory properties of *E.cuneatum* leaf alkaloid extract. Carrageenan-induced paw edema method was conducted on 42 male Sprague Dawley rats that were divided into six groups (n=7): positive control, negative control and four alkaloid extract groups with different doses of 5 mg/kg, 10 mg/kg, 25 mg/kg and 50 mg/kg respectively. 2% Tween 20 was administered to negative control group whereas 300 mg/kg aspirin was for positive control group. Rats were pretreated an hour before injection of carrageenan. Paws thickness was measured using vernier caliper every hour up to fifth hour upon induction. Histopathology examination of the induced paws was done by H&E stain and inflammatory scoring was conducted. The animals pretreated with *E.cuneatum* alkaloid extract demonstrated dose-dependent decrease in paw oedema upon subplantar injection of carrageenan as compared to negative control. The highest dose (50 mg/kg) alkaloid extract showed no significant difference of paw edema thickness as compared to positive control. Histopathologically, the highest dose of alkaloid extract showed significant reduction of leukocytes infiltration and collagen disruption as compared to negative control. In conclusion, this study showed that *E.cuneatum* possesses prophylactic anti-inflammatory properties against acute inflammation. The effect was in a dose-dependent manner in which 50 mg/kg of *E.cuneatum* alkaloid extract was the most effective dose to attenuate inflammation, similar to aspirin.

Keywords: *Erythroxylum cuneatum*, inflammation, carrageenan-induced paw oedema

POS049

Short-term Stability Study of Acyclovir-loaded Solid Lipid Nanoparticles

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Poor oral bioavailability of acyclovir has become one of the major drug delivery concerns globally. In order to improve current pharmacokinetic limitations of acyclovir, nanoparticulate system have been explored and exploited as its delivery vehicles. Nanoparticles offer many great advantages that include physicochemical stability and sustained-release properties. Stability test is one of the important measures of a successful development of nanocarrier and a pre-requisite for future clinical trials of a pharmaceutical product. In this study, we aimed to observe the physicochemical stability i.e size, zeta potential and polydispersity index of solid lipid nanoparticles suspensions loaded with acyclovir. Two different types of solid lipid were evaluated in this study; glyceryl dipalmitostearate (Biogapress Vegetal BM 297 ATO) and glyceryl dibehenate (Compritol 888 ATO), with polysorbate 80 (Tween 80) acted as emulsifying agent. After preparation of the acyclovir-loaded solid lipid nanoparticles based on the optimized formulations, the nanoparticles were stored at 4, 25 and 40 °C for a period of three months. All solid lipid nanoparticles containing acyclovir prepared from glyceryl dibehenate stored at 4 °C were considered stable throughout three months of testing period as no significant difference of particle size and polydispersity index were observed. Excellent particle's stabilization was achieved could be due to presence of free emulsifier in the suspension that prevent particle collision during storage at low temperature.

Keywords: stability studies, physicochemical stability, short-term test

POS050

Resting Salivary Flow Rate and pH Decreases in Chewable Tobacco Users

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Objective: The objective of the study was to find out the relationship between alterations in resting salivary flow rate (RSFR) and pH, which are early signs of oral health deterioration, with different forms of chewing tobacco products. **Design and Methods:** A total of 354 healthy male subjects, consuming any form of chewable tobacco, belonging to low socioeconomic areas of Karachi were selected for this cross sectional study. A questionnaire was used to collect demographic data and details of chewing habits (using since, pack/day, duration of exposure etc.). Resting saliva of every subject was collected for 5min and RSFR was expressed in ml/min. Salivary pH was determined by using pH strips (pH 0-14). Data was analyzed on SPSS version 20. **Results:** Of 354 subjects, 27.4% were gutka, 24.3% niswar, 24.3% paan and 24% multiple users with mean RSFR as 0.40 ± 0.30 , 0.65 ± 0.32 , 0.64 ± 0.39 and 0.41 ± 0.25 respectively. Mean resting salivary pH was 6.58 ± 0.78 with the lowest pH; 6.16 ± 0.65 in multiple users. RSFR and pH significantly decreased with increase in packs consumed/day, duration of exposure and duration of usage. **Conclusion:** A significant negative correlation was found between RSFR and pH with tobacco. A significant negative correlation was found between RSFR and pH with tobacco chewing.

Keywords: Saliva, Tobacco chewing, Resting Salivary flow rate, salivary pH

POS051

Comparative Osteoprotective Effects of *Labisia Pumila* Roots and Leaves in Ovariectomized Sprague-dawley Rats: A Pilot Study

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Objective: Estrogen replacement therapy (ERT), the gold standard treatment in postmenopausal osteoporosis, is known to cause several adverse effects. In search of a safer alternative, *Labisia pumila* var *alata* (LPva) has been reported to possess phytochemicals with estrogen-like biological activities (phytoestrogens) and protects bone of rat femur from changes associated with estrogen-deficiency. This study is aimed at comparing the osteoprotective effects of the root and leaf extracts of *Labisia pumila* var *alata* in ovariectomized rat model. **Design and Method:** Twenty-seven female rats were divided into nine groups (n=3): sham-operated (SHAM), ovariectomized control (OVXC), ovariectomized treated with 64.5 µg/kg dose of estrogen (OVXERT), ovariectomized treated with 20mg, 50mg and 100g/kg doses of LPva leaf extract (OVXLPV20, OVXLPV50, OVXLPV100) and ovariectomized treated with 20mg, 50mg and 100g/kg doses LPva root extract (OVXLPr20, OVXLPr50, OVXLPr100). After daily treatment for 8 weeks, right femur bones were excised and investigated for trabecular bone mineral density (BMD) and morphometric changes using Micro-computed tomography (Skyscan µ-CT). **Results:** To a similar extent as estrogen treatment group, significantly higher values of BMD, Trabecular number (Tb.N) and lower values of trabecular separation (Tb.Sp) were revealed in both the leaf and root extracts groups at 20 mg/kg dose when compared to ovariectomized control. However, the root extract group protected against changes in percentage bone volume (BV/TV) better than leaf extract and estrogen. **Conclusions:** Lower dose (20 mg/kg) of *Labisia pumila* var *alata* leaf and root extracts were more effective than higher doses (50 mg/kg and 100 mg/kg) in preserving BMD and trabecular bone Morphometry in post-menopausal conditions.

