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PLENARY 1

Omics, Inflammation and Gut

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Gut health influences the general well-being of human as it provides the core body's immune system. Environmental factors (exposome) such as diet, nutrients, smoking, obesity may interact with the intestinal microenvironment leading to multiple pathologies inside the gut. An inappropriate immune response towards environmental changes directing to oxidative stress in the mucosal layer of the GI tract. This will subsequently lead to inflammation and destruction in the intestinal mucosal. Inflammatory bowel disease (IBD), which is increasing steadily in the Asia pacific region, is a good example to explain these processes. In recent years, with the help of new high throughput technologies have enabled a better understanding on the genetic susceptibility of patients with IBD that interacts with the gut microbiota. The host-microbiota response will trigger the cell mediated inflammation causing the released of multiple cytokines. We have conducted transcriptomic profiling to understand the changes in the transcriptomes of long duration as compared to the short duration IBD patients. Differentially expressed genes include genes that are related with production of reactive oxygen species. Among the signaling pathway identified in this study was fatty acid metabolism, which is closely related to inflammation and IBD-related cancer (up to 20% of cancers arise from chronic inflammation). In daily routine, short chain fatty acids are produced by gut microbiota through fermentation of dietary fibers and resistant starch. Short chain fatty acids produced in colon may affect pro-inflammatory cytokines and enhance the migration of neutrophils to the inflammation site and helps in the process of phagocytosis. Our team has also shown the beneficial effects of modulating the gut immunity in post-operative patients with colorectal cancer as well as in patients with irritable bowel syndrome. With remarkable advanced in omics technology has reshaped the way we tackle gastrointestinal diseases.

PLENARY 2

Neuroinflammatory Mechanisms Involved in Alzheimer's Disease

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Inflammation has been considered as a pathological mechanism for Alzheimer's disease (AD) for more than 30 years, initially based on the pathological observations of activated microglia identified in postmortem human brains. In recent years, modern gene expression profiling techniques and single nucleotide polymorphism screening have been applied to identify different inflammation associated changes and new proteins involved. There have been discrepancies in the two approaches that need to be considered. Ultimately, the goals of all of these studies are to identify inflammation associated therapeutic targets for AD, but there is still incomplete understanding of how inflammation affects AD and the best way to modulate it. One approach is address the question 'what are microglia in AD brains *actually* doing". Comparison will be made between results from publicly available gene databases of AD and control human brain tissue, and immunohistochemical approaches using human brain tissues to phenotype microglial expression of key target proteins. Gene expression databases from human materials provide a wealth of information about inflammatory changes in AD brains with results conflicting with established concepts. To address the fundamental question about the extent and localization of activated microglia, we will consider the distribution of microglia expressing the purinergic receptor P2RY12 in relation to AD pathological structures. P2RY12 is considered a marker for non-activated microglia. In addition, genetic studies have linked triggering receptor expressed by myeloid cells-2 (TREM-2), CD33 and progranulin with inflammatory mechanisms of neurodegeneration. The expression of these proteins by microglia and their known biological functions will be considered in the context of AD inflammatory mechanisms. To understand and develop treatments for AD, an accurate picture of what is happening in human disease affected tissues is needed. This is needed to ensure that animal models used for testing therapies accurately reflect the human disease.

Keywords: Microglia, immunohistochemistry, gene expression, phenotypes, neurodegeneration

PLENARY 3

Is H_2O_2 Production Increased at High Mitochondrial Membrane Potential? Facts and Artefacts under Normoxia, Hyperoxia, and Hypoxia.

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Hydrogen peroxide (H_2O_2) production increases at high mitochondrial membrane potential in the resting state of LEAK-respiration relative to the ADP-activated OXPHOS state. This OXPHOS-LEAK paradigm of mitochondrial ROS production, however, is based on studies which typically ignore the fact that intracellular oxygen levels in the microenvironment of mitochondria are 'hypoxic' relative to environmental normoxia. Can the OXPHOS-LEAK-ROS paradigm be extended to physiological intracellular oxygen conditions? The Amplex UltraRed (AmR) assay is one of the most popular fluorescence methods for determination of mitochondrial and cellular net H_2O_2 flux. Quantitative and accurate measurement of ROS production, however, remains a critical issue. Quality control is required to avoid numerous artefacts. Independent of H_2O_2 flux, increasing fluorescence signals may result from photosensitive auto-oxidation of AmR, which represents a confounding chemical background process. What is fact and artefact in the fluorometric AmR assay under normoxia and hypoxia? H_2O_2 production and oxygen consumption were measured simultaneously in mitochondria isolated from mouse brain and heart, and in intact cells of *Saccharomyces cerevisiae*, using the O2k-FluoRespirometer (Oroboros Instruments, Austria) and four respiration media: Dulbecco's phosphate buffer saline (DBPS); KCl-based medium; respiratory media MiR05-Kit and Buffer z. Oxygen flux remained independent of oxygen concentration under normoxia and 'hypoxia'. In contrast, apparent H_2O_2 production increased significantly during repeated hypoxia/anoxia transitions of yeast suspended in DPBS. Such hypoxic peaks of H_2O_2 production, however, were revealed as an artefact of auto-oxidation in DBPS and KCl-based media, not observed in MiR05 and Buffer z. The actual H_2O_2 flux declined from normoxia to hypoxia and anoxia in intact yeast and isolated mitochondria in the active OXPHOS state stimulated by ADP, whereas H_2O_2 flux was constant from normoxia to hypoxia in the LEAK state in the absence

of stimulation by ADP. Taken together, our results (1) do not show any transient reductive oxidative stress under hypoxia, (2) suggest that mitochondrial H_2O_2 production is independent of respiratory activity in the OXPHOS or LEAK state under intracellular oxygen conditions, and thus (3) challenge the LEAK-OXPHOS-ROS paradigm, emphasizing the importance of controlling dissolved oxygen in the range of physiological intracellular conditions and avoiding artificially high oxygen levels in studies of ROS production.

SYMPOSIUM 1

Sequencing the Malaysian Human Genome

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Systematic investigation of human variation using genome sequencing approach is fundamental for the investigation of genetic risks towards diseases and how natural selection shapes the genetic architecture. Despite on-going research efforts, most diseases risks remained un-elucidated. In addition, these efforts covered populations from the major continents; population of Southeast Asia which is known to be genetically unique has not been systematically studied. We thus aimed to provide an in depth characterization of genome variations of the unique Orang Asli and the Malays. The outcomes of these studies will provide platforms for the development of models and algorithms for disease prediction and prevention, changing the paradigm of current medical practices via precision health. We have the largest Orang Asli whole genome database known to date. All the genomes were assembled and the variants were annotated using GATK Best Practice workflow, SIFT and Polyphen. The Orang Asli genomics architectures, SNPs associated with diseases and novel SNPs were identified. The Orang Asli have a total of 1276 non synonymous variants compared to 1938 among the Malays. The Orang Asli are genetically at risk towards diseases such as ADHD, CVD, leukemia, cancers and metabolic syndrome. Some of these genetic variations would be passed on from one generation to another and caused the gene pool to be weak and consequently may contribute to natural selection. This is of concern as Orang Asli discourage intermarriage. The rate of MetS was higher in several settlements in the suburban areas compared to the rural areas. Lifestyle intervention is urgently needed to prevent further deterioration of health among the Orang Asli. We had also successfully identified their talents to be athletes based on their sport genes. A substantial number of the Orang Asli carry endurance genes. We had developed genetic test kits for *HLA-B*15:02* and panels of targeted genes for detection of sport talents, metabolic diseases, sport genomics and nutrigenomics. We had proposed several strategies in our policy paper to the relevant authorities to ensure the survivability and sustainability of the Orang Asli in the Peninsular Malaysia.

SYMPOSIUM 2

Advances in Genomic Medicine and its Application

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The use of genomic information and technologies to study certain disease thoroughly for the optimal management of the condition is called genomic medicine. In general, the application of genomic medicine is effective in dealing with common monogenic diseases. The application of next generation sequencing (NGS) in tackling complex diseases including cancers is promising with the evidence of the cost of screening is lower than the cost of treating diseases themselves. However, it is more relevant to use genomic medicine to understand the genotype-phenotype relationship in complex diseases before an effective genomic risk identification, stratification and change in the management can be utilized in clinical practice. The application of genomics in studying reduction/oxidation homeostasis has shown a better understanding on the function and interactions of all genes in health and diseases. A surplus of reactive oxygen species can induce oxidative damage of macromolecules such as lipids and DNA, which is the basis of carcinogenesis process. The use of array-based methodologies or sequencing-based technologies have enabled scientists and clinicians to explore the roles of genomics, epigenetics, transcriptomics, metabolomics and the latest metagenomics to uncover the hypotheses of how body reacted to chronic stress. We are moving surely into a new revolutionary era of precision medicine. Generation of data is no longer a problem than interpret them. Undoubtedly, genomic medicine has remarkable potential to enhance human health. Tailoring appropriate medications based on pharmacokinetics, pharmacodynamics along with pharmacogenomics profiles will become a reality.

SYMPOSIUM 3

Brain Metabolomics Profiling in Aging and Alzheimer's disease

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Brain aging is a progressive and complex multifactorial process manifested by physiological and cognitive deterioration ultimately leading to death. Metabolites changes have been shown to be associated with brain aging and affecting the neuronal functions. Previous metabolomics studies have revealed the neurochemical changes that were associated with the progression of Alzheimer's disease (AD). We are interested to understand how the metabolites in the brain regions that associated with cognitive function are altered in the aging process. The level of metabolites was correlated with the behavioural changes to verify the molecular-functional relationship in the aging brain. The metabolomics data that was acquired in aging rats was further cross-checked with the Alzheimer's mouse model. Our findings provide the inputs on the interplay connection between brain metabolites and brain aging and Alzheimer's disease. Our findings suggest that brain metabolites are the important playmaker in the progression of brain aging as well as in the brain regions that are associated with Alzheimer's disease and, moreover the targeted metabolites shall be important biomarkers and possible targets in the management of aging and Alzheimer's disease.

SYMPOSIUM 4

Current Trends in Proteomics and its Applications in Studying Degenerative Diseases

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The term proteomics was first coined by Mark Wilkins in 1994. It is an area research of the "post-genomic era" and describes the global analysis of gene expression at the protein level in a multitude of samples. Since then, it has undergone an evolution from a heavy reliance on 2D gels (gel based proteomics) to depending more and more on liquid chromatography approaches coupled with mass spectrometry (gel free). Improvements in separation and mass spectrometry techniques have allowed proteomics experiments to be carried out with higher throughput and better reproducibility. In this talk, I will be discussing the various techniques and its merits/weaknesses. The suitability of each approach in obtaining different "types" of data will also be discussed. Specific examples in the use of these approaches in degenerative diseases will also be cited.

SYMPOSIUM 5

Potential Role of Small Molecule Inhibitors of Focal Adhesion Kinase in the Treatment of Stress and Inflammation Induced Glaucoma.

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Glaucoma is a leading cause of irreversible blindness worldwide with an estimated 80 million people affected by 2020. Despite having successful surgical procedures, there is a long-term graft failure and rejection because of ocular fibrosis and scarring resulting in blindness. The existing methods to prevent fibrosis after glaucoma surgery is to use the antimetabolites, mitomycin C (MMC) and 5-fluorouracil (5-FU). Although these antimetabolites improve the surgical outcome of glaucoma filtration surgery, they have non-specific cytotoxicity which potentially leads to blinding complications. In addition, not all patients are responsive to this antimetabolite therapy. There is a need to develop new anti-fibrotic therapeutics with more specific physiological actions and less cytotoxicity to inhibit the fibrosis and scarring observed following surgery for glaucoma. Most of the current drugs on the market acts by lowering IOP, yet the unmet need post-surgery is the precise control of tissue scarring and flow which is why we are proposing the use of a novel anti-fibrotic compound. Human and rabbit Tenon fibroblast were used for the *in vitro* study to look at the effect of the inhibitors on the FAK signalling pathway and the expression levels of pro-fibrotic genes. *In vivo* animal study was done using female New Zealand White rabbits subjected to glaucoma filtration surgery. Animals were given subconjunctival injections of either the inhibitor or buffer as control. This was done one day pre-operative, immediately post-operative and seven days daily post-operative. Clinical characteristics of the bleb appearance and intraocular pressure were recorded at set intervals. On day 29, the animals were sacrificed and both eyes enucleated and histologically analysed. In this study using the Human Tenon's Fibroblasts (HTFs) and Rabbit Tenon's Fibroblasts (RTFs) the small molecule inhibitors inhibited pY925 and pY-397 FAK phosphorylation as well as reducing the expression levels of pro-fibrotic markers. The anti-scarring effect of this compound is profound; it remains stable and effective prior to induction of fibrosis and active post-induction up to 7 days in *in vitro* studies. Animals treated with one of the

compound showed reduced fibrosis compared to the control animals. Inhibition of fibrosis significantly improved surgical outcome by reducing the amount of scar tissue produced. The anti-fibrosis inhibitors if proven successful in eye related disease will have great potential given the wide variety of fibrosis related diseases with large number of individuals suffering from devastating effect of fibrosis since there is currently yet to be an effective anti-fibrotic drug in the market. The main reason for this could be the lack of translational research and the big gap between basic research and technology development.

Keywords: Focal Adhesion Kinase, Fibrosis, Small molecule inhibitors, Glaucoma

SYMPOSIUM 6

Antioxidants and Neurodegenerative Diseases

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The brain is particularly susceptible to the effects of reactive oxygen species (ROS) due to its high metabolic rate and oxygen consumption but low amount of antioxidants. The oxidative damage leads to several neurodegenerative diseases including Alzheimer disease, Parkinson disease and amyotrophic lateral sclerosis (ALS). Thus antioxidants have been postulated to minimize or even prevent the progression of the neurodegeneration. *In vitro* studies have shown that free radicals cause apoptotic cell death in neurons but this can be prevented by treatment with several antioxidants such as vitamin E, *Centella asiatica, Momordica charantia, Piper bettle* and *Nigella sativa*. Animals supplemented with fruits and vegetables rich in antioxidants showed beneficial effects on age-related decline of neuronal and cognitive function in old rats. Curcumin, tea flavonoids (catechins), black tea extract, apple juice concentrate, L-carnitine, creatinine, co-enzyme Q10, lipoic acid, blueberry and spirulina are some of the antioxidants that were shown to protect against neurodegeneration in animal studies. We have shown that supplementation of old rats with centella asiatica and TRF reverses age-related cognitive deficit in rats. CA protects neuron cells via activation of the caspase-9 activity and inhibition of neuroinflammatory pathways. TRF supplementation have also been shown to reverse age-associated changes in arginine metabolites in the entorhinal cortex and cerebellum. Subsequent multiple regression analysis revealed a number of signicant neurochemical-behavioral correlations, indicating the beneficial effects of TRF supplementation on memory and motor function.

SYMPOSIUM 7

Corneal Healing: Exploring the Potential Therapeutic Modalities of Malaysian Honeys

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Cornea is an avascular and transparent tissue, which functions as the principal optical element and mechanical barrier to the eye. The use of topical antibiotics in treating corneal injury has been inundated with adverse effects such as resistance and delayed wound healing. Honey has long been proven to promote skin wound healing, but its effects on corneal healing has not been duly explored. The study aimed to determine the potential wound healing effects of Acacia and Gelam honeys on ex vivo corneal wound healing model. Corneal cells (epithelial and stromal keratocytes) were isolated from New Zealand White rabbits and cultured in Acacia- or Gelam honey-enriched medium in serial dilution. The optimal dose of the honeys was determined via MTT assay and phenotypic characterization of both cells were conducted. Ex vivo corneal ulceration using 4 mm corneal trephine was created onto the confluent cells. Wound healing assays, genes and immunohistochemistry of healing and scarring markers were assessed. Optimal dose of Gelam and Acacia honeys in promoting proliferation was 0.0015% and 0.025% respectively. Complete wound closure was attained in both cells at day 5 in Gelam honey-enriched medium compared to day 6 in Acacia honey-enriched medium. The addition of honeys potentiate the expression of healing markers and reduction in scarring markers while retaining the corneal epithelial and stromal keratocytes phenotypes. In conclusion, supplementation of Gelam and Acacia honeys were able to promote corneal cell proliferation, migration and healing in the ex vivo corneal ulcer model. These positive effects could serve as an enormous potential of Malaysian honeys as nutripharmaceutical agent in corneal wound healing.

Keywords: Cornea, wound healing, ex vivo ulcer model, Gelam Honey, Acacia Honey.

SYMPOSIUM 8

Hormone Therapy in Brain Aging and Alzheimer's Disease

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Gonadal steroid hormones such as estrogen and progesterone exert their effects well beyond the traditional held confines of reproductive function. Indeed, these hormones now have well documented effects on numerous tissues and organ systems, including the brain. Given that estrogen and progesterone have important physiological effects on the brain, it is critical to understand the consequence of long term hormone deprivation since women can now expect to live approximately a third of their lives after the menopausal transition, a period in a woman's life that is associated with a precipitous decline in estrogen and progesterone levels. Indeed, it is the negative consequences of ovarian steroid hormone deprivation, that occurs following ovariectomy or the menopause, that have collectively served as the foundation for considering hormone (replacement) therapy as a potential means of keeping the brain healthy and staving off such age-associated diseases as Alzheimer's disease. Here, we review the data that demonstrate the negative consequences of ovariectomy on cognitive function and relevant biochemical and molecular mechanisms that serve to support cognitive resiliency and health. Further, we highlight the fact that though significant attention has been placed on the neuroprotective role of estrogens, it is important to consider that ovariectomy, like the menopause, results in the precipitous loss of not only estrogen but of progesterone as well. As such, the loss of progesterone may contribute to the deficits observed after ovariectomy or the increased risk for Alzheimer's disease seen after the menopause. Indeed, recent evidence supports the neuroprotective potential of progesterone itself, and review our current understanding of some of the diverse mechanisms by which progesterone may reduce neuronal vulnerability to toxic insults relevant to age and age-associated diseases such as Alzheimer's disease.

SYMPOSIUM 9

A Thai Traditional Polyherbal Tonic, Jatu-Phala-Tiga, Exerts Antioxidant Activities and Extends Lifespan in *Caenorhabditis elegans*

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The imbalance between the generation of free radicals and natural cellular antioxidant defenses, known as oxidative stress, can cause oxidation of biomolecules and further contribute to aging-associated diseases. Plant-derived compounds have been extensively considered as effective sources of antioxidants. The aim of this study was to evaluate the antioxidant capacities of a traditional polyherbal tonic, Jatu-Phala-Tiga (JPT) and its herbal ingredients consisting of *Phyllanthus emblica*, *Terminalia arjuna*, *Terminalia chebula*, and *Terminalia bellirica*. The effect of JPT on the lifespan of *Caenorhabditis elegans* were additionally described. Among the extracts, JPT water extract exerted remarkable antioxidant activities as compared to the extracts from other solvents and individual constituting plant extract. JPT water extract was found to possess the highest metal chelating activity, with an IC_{50} value of 1.75 ± 0.05 mg/mL. Moreover, it exhibited remarkable scavenging activities towards DPPH, ABTS, and superoxide anion radicals, with IC_{50} values of 0.31 ± 0.02, 0.308 ± 0.004, and 0.055 ± 0.002 mg/mL, respectively. The ORAC and FRAP values of JPT water extract were 40.338 ± 2.273 µM of Trolox/µg of extract and 23.07 ± 1.84 mM $FeSO_4$/mg sample, respectively. Treatment with JPT water extract at 5 mg/mL increased *C. elegans* lifespan under normal growth condition (15.50 ± 0.07 *vs.* 21.00 ± 1.41 days; $p<0.05$) and H_2O_2-induced oxidative stress condition (14.33 ± 0.58 *vs.* 16.67 ± 0.40 days; $p<0.05$). The results indicated that JPT and its herbal ingredients exhibited strong antioxidant activities, in particular the water extract of the polyherbal tonic. These findings rationalize further investigation in JPT water extract as a promising agent for anti-aging and oxidative stress prevention.

Keywords: Antioxidants, Polyherbal formula, Herbal tonic, *Caenorhabditis elegans*

SYMPOSIUM 10

Glaucoma and Oxidative Stress: Is There a Connection and Potential New Therapy?

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Glaucoma is one of the causes of irreversible blindness in the world. Blindness due to the glaucoma is a major concern in Asia. However, the pathogenesis of glaucoma is still unknown. Mechanical theory used to be the leading postulated theory; direct mechanical pressure to the optic nerve head responsible for optic neuropathy. Advancement of research tools, non-mechanical theory including oxidative stress has generated new interest. Experimental research outcome including the in-vivo and in-vitro findings will be highlighted to look for potential link between glaucoma and oxidative stress. Clinically, the evidence of the level and type of oxidative stress markers in ocular fluid and serum will be reviewed as potential detection tool. Potential therapy including free radical scavengers in our food, glaucoma drugs and herbs will also be discussed.

SYMPOSIUM 11

Mitochondrial Dysfunction in Alzheimer's Disease and Its Modulation by Tocopherol Isomer

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Clinical trials have shown that vitamin E supplementation improves cognitive performance and delays the progression of Alzheimer's disease. The mechanism of action of vitamin E in improving cognitive function has been widely studied but its effect on mitochondrial function is still poorly understood. This study established three neuroblastoma cell models of SH-SY5Y stably expressing wild-type (SH-SY5Y-APP WT), single-mutant Swedish (SH-SY5Y-APP Swe) and double-mutant Swedish/Indiana (SH-SY5Y APP Swe/Ind) forms of APP gene which produces high level of amyloid-beta (Aβ) in an attempt to determine the effect of tocopherol isomers on mitochondrial function in Alzheimer's disease (AD). The ratio of Aβ42/Aβ40 was measured for verification of the established stable cell models as it gives better diagnostic performance in AD than the level of certain type of Aβ alone. The levels of ATP and reactive oxygen species (ROS), respiration rate, mitochondrial membrane potential, activity of complex IV and V enzymes, cytochrome c release, and protein expression involved in regulating mitochondrial permeability transition pore (mPTP) and apoptosis were determined with and without treatment of α-tocopherol (ATF) (5, 100 μM) and γ-tocopherol (GTF) (5, 80 μM). Our results showed that the ratio of Aβ42/Aβ40 protein increased in the following order; SH-SY5Y-APP WT <SH-SY5Y-APP Swe <SH-SY5Y APP Swe/Ind. Mitochondrial functions such as respiration rate (ROUTINE, $OXPHOS_{CI\text{-}CII\text{-}LINKED}$ and ETS), complex IV and V activities, and membrane potential ($OXPHOS_{CI\text{-}CII\text{-}LINKED,}$ $LEAK_{PM,}$ $OXPHOS_{CI\text{-}LINKED}$ and ETS) were significantly different in the different AD models studied. A similar result was observed for mitochondrial ROS level. Protein expression of CypD, ratio of BAX/Bcl2 and pro-caspase 3 was also differently expressed in different *in vitro* models of AD. Cytocrome c release however was increased only in mutant cells. Treatment with tocopherol isomers was found to improve mitochondrial functions as shown by increased ATP level, decreased mitochondrial ROS level, and improved complex IV and V activities. Both ATF and GTF modulated mitochondrial respiration and membrane potential differently at different respiration state and cell types. Furthermore, treatment with GTF decreased the proteins expression of CypD,

cytochrome c, ratio of BAX/Bcl2 and pro-caspase 3 while ATF only decreased protein BAX/Bcl2 ratio in all transfected cells. In conclusion, high Aβ without APP mutation alters several mitochondrial functions and this effect was more severe in the presence of APP mutation. Treatment with tocopherol isomers especially GTF restored mitochondrial function that may prevent the opening of mPTP and apoptosis event thus, delays the progression of Alzheimer's disease.

Keywords: Tocopherol, amyloid precursor protein, mitochondrial functions, apoptosis, Alzheimer's disease

SYMPOSIUM 12

Control of Mitochondrial DNA Integrity in Ageing and Diseases

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There are various quality control (QC) pathways which form a complex network to ensure functional integrity of individual biological cellular units inclusive of the mitochondria; impairments within this intricate network will result in ageing and disease state. The mitochondria which is involved in various essential functions including energy transduction require an efficient QC as they have the potential to generate superoxide anion radical which may be converted to other ROS; the latter if present in high levels is toxic to virtually all biomolecules. Mitochondrial mutations and mtDNA rearrangements accumulate with ageing; the process of increasing heteroplasmy with time is called clonal expansion and might occur as a result of selective advantage of damaged DNA over healthy DNA. It has been shown that various heteroplasmy threshold exists in manifestation of different diseases. In order to prevent deleterious effects of these mutations, cells may either repair arising mtDNA mutations by mitochondrial base excision repair (mtBER) pathway or shift the heteroplasmy of existing mutations below the phenotypic threshold by means of mtDNA copy number regulation; the latter is achieved by targeted degradation of damaged mtDNA molecules or increased mtDNA replication of wild type molecules. Impairment in pathways involved in proteostasis also impacts on mitochondrial integrity leading to degenerative processes. Mitochondrial dynamics which comprise the process of fusion and fission also works to maintain mitochondrial function and quality control. Finally, selective autophagy and programmed cell death (apoptosis) also facilitates in elimination of severely damaged cells. Better understanding of all these underlying mechanisms are essential for the development of targeted interventions for mitochondrial dysfunctions, degenerative processes, ageing and age-related diseases resulting from impairment of mitochondria.

SYMPOSIUM 13

Mitochondrial Function Abnormalities in Idiopathic Autism Spectrum Disorder

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Autism spectrum disorders (ASD) are a heterogeneous group of neurodevelopmental disorders defined by impairments in communication and social interactions along with restrictive and repetitive behaviours. These symptoms become apparent only at the age of 2. There is currently no cure for autism and medical therapy is limited to targeting behavioural symptoms. Although the underlying cause of autism is unknown, a growing body of clinical, genetic, and biochemical evidence now proposed that impaired mitochondrial function may be linked to the diverse medical symptoms associated with idiopathic ASDs. The mitochondrial function and respiration of the lymphoblastoid cell line derived from children with idiopathic autism (ALCL), and their developmentally normal siblings (NALCL) were measured using high-resolution respirometry, Oxygraph-2k (O2k). Our results showed that the OXPHOS capacity (P) and ETS capacity (E) in ALCL were significantly higher compared to NALCL ($p<0.01$). In an experiment measuring the CII-linked respiration rate and mitochondrial membrane potential (MMP) simultaneously, the CII-linked P and E were higher in ALCL compared to NALCL ($p<0.01$) although MMP did not show any significant difference between the two states of respiration. In addition, complex IV activity was also found to be higher in ALCL as compared to NALCL ($p<01$). The overall activity in ATP generating pathway in autism cells was higher than in the normal siblings except for the MMP. These findings proposed that abnormalities in mitochondrial function might play a significant role in the pathogenesis of ASD.

Keywords: Autism, mitochondria, oxidative stress, OXPHOS, electron transport system

SYMPOSIUM 14

Shape-Shifters in The Heart: Heralding A New Era of Mitochondrial Medicine. Or Not?

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Cardiovascular disorders remain the main cause of mortality and morbidity worldwide. As such, novel therapeutic strategies are essential to improve patients' prognosis and outcomes. Imbalances in cardiac mitochondrial morphology (shapes) have been discovered to be a hallmark feature in perturbations to optimal cardiac physiology. Modulating cardiac mitochondrial morphology thus constitutes a novel therapeutic strategy to combating cardiovascular disorders. Nonetheless, further investigations are needed to fully comprehend the dynamism of cardiac mitochondrial morphology alongside the quest for compounds that specifically target the mitochondrial morphology. In this talk, I will describe the ongoing efforts in my laboratory focusing on cardiac mitochondrial dynamics as a novel therapeutic target against cardiovascular disorders.

FR001

Age-related Alteration in the Proteome Profile of Rat Brain

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Background: Brain aging is a complex multifactorial process accompanied by physiological and cognitive deteriorations that ultimately lead to death. We have recently shown that age-dependent regional brain atrophy and lateral ventricle expansion may be linked with impaired cognitive and locomotor functions in rats. However, proteomic alterations in various brain regions during aging is still unknown. Therefore, this study is sought to determine the effect of aging on the brain proteome of middle- to late-aged rats.
Methods: Sprague Dawley rats aged 14 (n=14), 18 (n=13), 23 (n=7), and 27 (n=10) months old were used in this study. Proteomic analysis was performed on the rat hippocampus, medial prefrontal cortex, and striatum using ultrahigh performance liquid chromatography coupled to Q Exactive HF Orbitrap mass spectrometry. The recorded data were further analysed using bioinformatics approach for identification and quantification of the proteins. The altered proteins were classified into three ontologies (cellular component, molecular function, and biological process). The proteins were then mapped to Kyoto Encyclopedia of Genes and Genomes database.
Results: Proteomic analysis suggested that the altered proteins were brain region-specific. Hippocampus was the most affected region with aging. Bioinformatics analysis revealed that these proteins were mostly localized in cell and organelle, primarily involved in binding and catalytic activity, and also metabolic activities. These proteins were mostly participated in oxidative phosphorylation, glutathione metabolism, and calcium signaling pathway.
Conclusion: Aging-induced alterations in various protein characteristic simplicate several vital cellular pathways such as oxidative phosphorylation, glutathione metabolism, and calcium signaling, that may mediate cognitive and locomotor impairments.

Keywords: Aging, Brain, Proteomics

FR002

Impact of Tocotrienol-Rich Fraction Supplementation on the Ovarian Metabolome and Quality of Oocytes in Aging Mice

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Background: Ovarian aging has been associated with increased oxidative stress and eventual loss ofovarian function. Ovarian aging is accompanied by a decrease in quality of oocytes and infertility. Tocotrienol, a potent antioxidant has been proven to exert beneficial effects on female reproductive system. The relationship between metabolomic changes in ovary and the quality of oocytes in aging mice following tocotrienol-rich fraction (TRF) supplementation was investigated.
Methods: Six-month-old female mice (Mus musculus) were divided into four groups. First group was given tocopherol-stripped corn oil (vehicle control) while the other three groups were supplemented orally with TRF at doses of 90, 120, and 150 mg/kg for two months, respectively. After two months, mice from all groups were superovulated and euthanised. The quality of oocytes was assessed and non-targeted metabolomics analysis was performed on the ovarian tissues.
Results: Percentages of normal oocytes were significantly higher ($p<0.001$) while fragmented oocytes were significantly lower ($p<0.001$) in all TRF supplemented groups as compared to the control. Using non-targeted metabolomics methods, thousands of metabolite signals were captured whereby 40 metabolites were identified to be different in the ovarian tissue of vehicle control and TRF supplemented groups. Significant changes were detected in metabolic pathways that include fatty acids, amino acids metabolism and steroid hormone biosynthesis.
Conclusion: Taken together, our results suggest that TRF exerts a protective mechanism towards female reproductive aging.

Keywords: Metabolomics, ovary, oocyte, aging, female reproductive system

FR003

Attenuation of Neuroinflammation and Caspase-3 Activity by Tualang Honey in Kainic Acid-Induced Excitotoxicity Rat Model

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Background: Excitotoxicity is a major mechanism of neuronal cell death in the neurodegenerative diseases. Neuroinflammation and apoptosis play an important role in the pathogenesis and progression of neurodegeneration. Systemic injection of kainic acid (KA) can induce neuroinflammation and apoptosis, resulting in the neurodegeneration in the selective brain regions of rodents. This study focused on the possible anti-inflammatory and anti-apoptotic effects of Malaysian Tualang Honey (TH) against kainic acid (KA)-induced excitotoxicity in rat cerebral cortex, cerebellum, and brainstem.

Methods: Male Sprague-Dawley rats were divided into four groups as Control, KA-treated, TH + KA-treated, and Topiramate (TPM–antiepileptic agent) + KA-treated groups. Control and KA-treated groups were pre-treated orally with drinking water, whereas TH + KA-treated and TPM + KA-treated groups pre-treated orally with TH (1.0g/kg BW) and TPM (40mg/kg BW), respectively, once every 12 h for five times. KA (15mg/kg BW) was injected subcutaneously 30 min after last treatment to all groups except the control group (normal saline). Animals were then sacrificed at 2, 24 or 48 h after KA administration. Neuroinflammatory markers and caspase-3 activity were analysed in rat cerebral cortex, cerebellum, and brainstem.

Results: Administration of KA caused significant ($p<0.05$) increase in the levels of glial fibrillary acidic protein (GFAP), ionized calcium-binding adapter molecule 1 (Iba-1) and cyclooxygenase-2 (COX-2) and activity of caspase-3 in the selective brain regions and time points. Pretreatment with TH significantly ($p<0.05$) reduced the increase of GFAP, AIF-1 and COX-2 levels in the selective brain regions and time points and the increase of caspase-3 activity in the cerebral cortex at all time points. The results demonstrate that TH mediated its neuroprotection against KA-induced excitotoxicity through attenuation of neuroinflammation and caspase-3 activity in the selective brain regions and time points.

Conclusion: It was concluded that TH may provide a potential therapeutic strategy for the treatment of progressive neurodegenerative disease by ameliorating the neuroinflammation and apoptosis.

Keywords: Kainic Acid, Excitotoxicity, Neuroinflammation, Caspase-3, Tualang Honey

FR004

Core Stability and Hip Stability of Knee Osteoarthritis Patients

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Background: Knees, hip and core body play a significant role in supporting the body weight in any weight bearing movement, thus core stability and hip stability could contribute to knee osteoarthritis (OA). Therefore, this study was carried out to determine the core stability and hip stability of knee OA patients.
Methods: A total of thirty-two women aged between 45 to 60 years have volunteered to participate in this study, comprising 16 knee OA patients and 16 normal. The core stability was assessed using core muscle endurance, core muscle strength and core muscle flexibility. Hip crossover test was used to see differences in hip stability.
Results: Data of core muscle strength, flexibility and hip stability were analyzed using chi square; and core muscle endurance data was analyzed using independent sample t-test and spearman rho correlation. This study found that knee OA patients have poor core muscle strength [*trunk curl* (χ=13.622, p=0.003); *lunges* (χ=13.833, p=0.003); *single leg squat* (χ=19.143, p=0.000) and squats (χ=17.622, p=0.001)]; core muscle endurance [*plank endurance* (z=-3.696, p=0.000); *side bridge (*z=-4.294, p=0.000); *flexor endurance* (z=-3.909, p=0.000); and *back extensor* (z=-2.504, p=0.012)]; core muscle flexibility [*Ely's test* (chi=15.393, p=0.000)]; and hip stability [Hip Crossover Test (χ=8.000, p=0.005)] as compared to normal subjects.
Conclusion: The core stability and hip stability of knee OA patients appeared to be significantly weaker than normal subjects. Thus, core stability and hip stability training have high potential not only to lessen the symptoms of knee osteoarthritis, but to improve the functional movement of knee OA patients and also to reduce the risk of knee OA among women.

Keywords: Core stability, hip stability, knee osteoarthritis.

FR005

The Antioxidative and Anti-inflammatory Effects of *Gynuraprocumbens*.

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Background: Atherosclerosis is one of the main causes of cardiovascular diseases such as coronary heart disease and stroke. The pathophysiology of atherosclerosis includes oxidative stress and inflammation. *Gynura procumbens* (Asteraceae) or Sambung Nyawa is an edible plant that has been used traditionally to treat various ailments such as pain, fever, rheumatism and kidney problem. Previous studies reported that the plant exhibit antioxidant, antibacterial, anti-inflammatory and anticancer potential. This study was aimed to investigate the effect of *G. procumbens* extract on lipid peroxidation of low density lipoprotein, nitric oxide production and proinflammatory adhesion molecules expression.
Methods: The effect of *G. procumbens* extract on lipid peroxidation of low density lipoprotein, nitric oxide production and adhesion molecules expression was determined using malondialdehyde (MDA) assay, Griess assay and Western blotting.
Results: *G. procumbens* extract inhibited lipid peroxidation of low density lipoprotein in a concentration dependent manner. The extract also reversed the suppression of nitric oxide production by N(G)-Nitro-L-arginine methyl ester and inhibited intracellular adhesion molecule-1 and vascular cell adhesion molecule-1 protein expression by tumor necrosis factor-α.
Conclusion: *G. procumbens* extract inhibits lipid peroxidation, production of nitric oxide, and adhesion molecules in endothelial cells, which corroborates it's potential in prevention of atherosclerosis.

Keywords: Atherosclerosis, *Gynura procumbens*, lipid peroxidation, nitric oxide, adhesion molecule

FR006

Validation of a Rodent Model of Ethanol Withdrawal

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Background: To date, various modes of ethanol administration have been experimented in animals to mimic human condition of alcoholism. Liquid diet technique is one of the most relevant methods that could induce behavioural and biochemical changes comparable to chronic alcoholism, which include marked increase in blood ethanol level and manifestation of withdrawal symptoms upon cessation of ethanol intake.
Methods: 24 Male Wistar rats were given a modified liquid diet (MLD) containing low fat cow's milk, sucrose, and maltodextrin with gradual introduction of 2.4%, 4.8% and 7.2% ethanol for 20 days. The rats' body weight and amount of MLD consumed was recorded daily. Following 20 days of chronic ethanol administration, ethanol was removed from MLD and replaced with isocaloric carbohydrate. The rats were then observed at every hour for 12 hours from the time of withdrawal, for the manifestation of ethanol withdrawal (EW) symptoms such as abnormal posture, abnormal gait, agitation, tail stiffness, stereotyped behaviours, and tremors. During the abstinence, the rats were treated intraperitoneally with normal saline and ethanol (2.5g/kg, 20% w/v) at 6th hours into withdrawal. Prior to induction of abstinence, the rats' sera was collected for analysis of ethanol level.
Results: A steady increase in most of the EW score was noticed during the abstinence from hour one until hour seven, while tail stiffness was observed at hour nine from withdrawal. Administration of acute ethanol significantly reduced the EW-induced behavioural changes, mostly from hour seven until twelve. As for tail stiffness, significant decrease was seen at nineth hour following acute ethanol challenge. The mean sera ethanol level of EW rats was 283.11 ± 18.43 $mgdl^{-1}$.
Conclusion: Manifestation of withdrawal symptoms following the cessation of ethanol intake and high blood ethanol level upon prolonged drinking validates the use of the MLD for the development of EW in rats.

Keywords: Ethanol withdrawal, liquid diet

FR007

Core Body Resistance Exercise Improves Lower Extremity Motor Function among Stroke Survivors

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Introduction: Weakness on core muscles occurred bilaterally after a stroke. This causes a compromise on motor functions. Therefore, this study was conducted to examine the effects of core body resistance exercises on lower extremity motor functions in strokes.

Methods: Thirty-four patients, aged 47.74±13.162 years old, were selected from Queen Elizabeth I and Tuaran Hospitals in Sabah, Malaysia. Patients underwent supervised core body resistance exercises which were prescribed specifically depending on patient's motor ability, twice weekly for total of 12 weeks intervention. Evaluation of motor function was carried out at baseline and every 6thweek interval for total of 18 weeks, using Fugl-Meyer Assessment Lower Extremity (FMA-LE), which consists of 4 domains: Motor function (LEMF), Sensation (S), Passive joint motion (PJM) and Joint pain (JP). Repeated measures ANOVA and paired t-test were used to analyse the effect of core body resistance exercise on lower extremity motor function.

Results: The effect of treatment across time improve significantly for lower extremity motor function, $F(3,99)=33.541$, $p=0.000$, passive joint motion, $F(2.108, 69.557)=42.577$, $p=0.000$ and joint pain, $F(1.663, 54.876)=9.064$, $p=0.01$ except for sensation, $F(2.301,75.937)=2.542$, $p=0.78$. However, the pre and post data analysis showed significant improvement in all four domains: lower extremity motor function [LEMFpre=11.2353±6.11535, LEMFpost=18.3235±6.7542, $t(33)=-10.990$, $p=0.000$], PJMpre=10.71±5.458, passive joint motion [PJMpost=17.53±2.842; $t(33)=-8.501$; $p=0.000$], joint pain [JPpre=15.76±5.657, JPpost=19.00±1.723; $t(33)=-3.674$, $p=0.001$] and sensation [Spre=7.97±4.239, Spost=9.24±3.652; $t(33)=-2.219$; $p=0.034$]. The level of significant was set at $p<0.005$.

Conclusion: These results suggested that core body resistance exercises may be used to improved lower extremity motor functions in strokes, and it can also be used to enhance passive joint motion and joint pain as well as the sensation. However, more specific treatment for sensation needed for better improvement.

Keywords: Stroke, lower extremity, motor function, coordination, core body exercise

FR008

Mitochondrial Changes in Cardiomyogenic Induced Mesenchymal Stem Cells in Rescuing Ischemic Cardiomyocytes

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Background: Ischemic heart disease (IHD) is the main cause of mortality globally. Alterations of mitochondrial structure and function are initiated by compromise myocardial due to IHD. It had been shown that mesenchymal stem cells (MSCs) can be induced to express cardiomyogenic markers and hence postulate their possible use to regenerate infarcted heart muscles. Along with the commitment to cardiomyogenic lineage, maturation of mitochondria with morphological and functional changes, enable these cells to rescue ischemic cardiomyocytes via mitochondrial donation. Our aim was to explore the possible role of direct cell-to-cell interaction between ischemic human cardiomyocytes and cardiomyogenic induced MSCs via tunneling nanotubes (TNT) formation or permanent cell fusion in order to transfer mitochondria to rescue ischemic cardiomyocytes.
Methods: MSCs were differentiated using optimized induction methods into cardiomyogenic lineage. Transmission electron microscopy was performed to examine the mitochondrial morphology and subsequently cellular ATP content was quantified. Co-culture of cardiomyogenic induced MSCs using an optimized *in vitro* model of cardiac ischemia was performed to evaluate the rescue mechanisms via mitochondrial donation.
Results: Morphology of the mitochondria was significantly different in terms of area, perimeter, circularity and elongation between non-induced and cardiomyogenic induced MSCs. These morphological changes were correlated with increment in ATP production. The survival of ischemic cardiomyocytes that were co-cultured with cardiomyogenic induced MSCs (39.27$\pm$0.28%) was significantly higher compared to the non-induced MSCs (29.57$\pm$1.46%) and non-treated group (14.09$\pm$0.16%) ($p<0.0001$). These results validated the advantages of using cardiomyogenic induced MSCs for increasing the survival of ischemic cardiomyocytes via mitochondrial donation through TNT formation and cell fusion.

Conclusion: Cardiomyogenic induced MSCs stimulates the morphological and bioenergetics maturation of mitochondria. Co-culturing of ischemic cardiomyocytes and cardiomyogenic induced MSCs demonstrated improved *in vitro* survival rate of injured cardiomyocytes via mitochondrial donation and restore their energy level to meet the energy demand.

Keywords: ATP, human bone marrow mesenchymal stem cell, mitochondria, cardiomyocytes rescue

FR009

A Case-control Study and Meta-analysis on Association of *eNOS* rs1799983 SNP with Stroke Risk

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Background: The endothelial nitric oxide synthase (*eNOS*) rs1799983 polymorphism has been known to increase the risk towards stroke, but data is underreported in Malaysian. Therefore, this study sought to investigate this association in a Malaysian population and in a comprehensive meta-analysis.
Methods: Genotyping of *eNOS* rs1799983 polymorphism was performed for 241 Malaysians using a hydrolysis probe. Odd ratio with 95% confidence interval was calculated. Meta-analysis was conducted using the Comprehensive Meta Analysis software Ver. 2.2.064. A *p*-value less than 0.05 was considered statistically significant.
Results: Overall, our results showed that the *eNOS* rs1799983-GT genotype increases the risk towards stroke particularly in male subjects and fast food goers. The meta-analysis showed that the rs1799983 polymorphism is significantly associated with an increase ischemic stroke risk in the recessive and allelic models. After stratified with population, these associations remain significant in the Asian population but not in the Caucasian population.
Conclusion: This study established a significant relationship between *eNOS* rs1799983 polymorphism with gender and lifestyle differences towards stroke risk in the Malaysian population. In addition, our metaanalysis suggested that the *eNOS* rs1799983 polymorphism was associated with an increased risk of ischemic stroke.

Keywords: *eNOS*, rs1799983, SNP, stroke, meta-analysis

FR010

Glucomoringin-isothiocyanate (GMG-ITC) Preserved the Integrity of Cellular Structures in an *In Vitro* Model of Neurodegeneration

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Background: Reactive oxygen species (ROS) are known to induce oxidative stress-related conditions. They oxidize important cellular markers via series of signal transductions resulting to devastative effects on the host organs with consequent death of cells through apoptotic and/or necrotic processes. The resulting effect(s) are thought to be associated with pathological changes perceived in a number of neurodegenerative disease conditions. Previous studies have shown that hydrolytic product of various glucosinolates isolated from cruciferous vegetables exhibited strong antioxidant activities in neuron cells protecting them from being degenerated. As such, the aim of this study was to investigate the neuroprotective ability of a bioactive compound glucomoringin-isothiocyanate (GMG-ITC) isolated from *Moringa oleifera* seeds in H_2O_2-induced neuroblastoma cells SHSY5Y.
Methods: The neuroprotective ability of GMG-ITC was carried out on all trans retinoic acid (RA) induced-differentiated human neuroblastoma cells (SHSY5Y) by the determination of cell viability assay, live and death cells analysis, ROS generation assay and surface morphological integrity. Ultrastructural analysis was also performed using scanning and transmission electron microscopy to assess the orientation of surface and internal features of GMG-ITC treated neuronal cells.
Results: ROS generation in neuroblastaoma cells SHSY5Y was reduced upon GMG-ITC pre-treatment in H_2O_2 induced SHSY5Ycells indicating mitigation of the intracellular oxidative stress. A remarkable protection of cell surface integrity and cytoplasmic inclusions was also overserved in the GMG-ITC pre-treated neuron cells.
Conclusion: GMG-ITC has a robust potential to prevent neuronal degeneration

induced by oxidative-stress related cytotoxic processes.

Keywords: Apoptosis, glucomoringin-isothiocyanate, human neuroblastoma cells, *Moringa oleifera,* neuronal differentiation, neurodegeneration.

FR011

Gynura procumbens Alleviates Vascular Inflammation and Increases Vascular Reactivity in Atherosclerosis Rat Model

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Background: Atherosclerosis is the major risk factor for cardiovascular disease. *Gynura procumbens (Lour.) Merr.* has been reported to have anti-hyperlipidaemic, hypertensive, antioxidative, and anti-hyperglycemic properties. To date, there is no research studied on its effect to prevent atherosclerosis development. Therefore, this study aims to determine the effect of *G. procumbens* in measuring inflammatory biomarkers and vascular reactivity in atherosclerotic rat model.

Methods: Forty-eight female Sprague Dawley (SD) rats were randomly divided into eight groups as follows; sham with (1) basal diet, (2) 250G.procumbens; (3) 500G.procumbens; (4) atorvastatin (ATV); and atherosclerotic rat model with (5) 2%CHO5HPO; (6) 2%CHO5HPO250G.procumbens; (7) 2%CHO5HPO500G. procumbens; (8) 2%CHO5HPOATV. Treatment was given for 24 weeks. Blood pressure was measured at baseline and at monthly interval of six months. Inflammatory biomarkers (IL-6, TNF-α and CRP) in plasma was determined using commercially available ELISA kit (Elabscience Biotechnology, USA). Rat were sacrificed and thoracic aorta were isolated for measurement of vascular reactivity.

Results: The increase in blood pressure starting from duration time of 0 to 6th months were associated with an increase in IL-6, TNF-α and CRP level in plasma of atherosclerotic group (2%CHO5HPO) and reduced with *G. procumbens* extract supplementation at 250 and 500 mg/kg body weight. Vasodilator response to Ach and SNP was significantly lower ($p<0.05$) in 2%CHO5HPO but increase with supplementation of *G. procumbens* extract. Aortic ring in treatment with *G.procumbens* extract supplementation were susceptible in response to PE by increase the contraction activity.

Conclusion: *G. procumbens* extract supplementation with the dose of 500 mg/kg body weight gave better effect than the lower dose (250 mg/kg body weight) in blood pressure control and it is reflected in IL-6, TNF-α and CRP levels. Standardized extract of *G. procumbens* has the ability to control the vascular tone and improve

the impaired endothelial function in atherosclerotic condition.

Keywords: *Gynura procumbens*, inflammatory biomarkers, IL-6, CRP, TNF-α, vascular reactivity, atherosclerosis.

FR012

The Effects of Activities of Daily Living (ADL) Balance Training on Functional Balance Impairment in Strokes

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Introduction: Functional balance is often impaired following a stroke and affects patient's functional ability due to poor muscle strength and control. Therefore, balance training is a critical component of stroke rehabilitation. Studies had shown that changes in balance function are highly correlated with recovery in ambulation and ADL function. The aim of this study was to evaluate the effects of ADL balance training on functional balance in stroke survivors.
Methodology: Twenty-two patients with unilateral hemiparesis, aged 24 to 74 years old, were selected from Queen Elizabeth I and Tuaran Hospitals in Sabah, Malaysia. Patients carried out a 2-hour, once a week ADL balance training 12 weeks intervention. This involved stages of functional balance activities from static sitting (SSt), dynamic sitting (DSt), static standing (SSd), dynamic standing (DSd), transfer (T), mobility activities (MA) and stepping activites (SA). The functional balance was evaluated from baseline, at every third week until 18th week of the program, using Brunel Balance Assessment (BBA), consisting of hierarchical series of performance tests which were divided into four sections of 12-level categories: sitting (level 1-3), standing (level 4-8), walking (level 9-10) and stepping (11-12). Repeated measures ANOVA and paired t-test was conducted to analyse the effect of ADL balance training on functional balance in stroke survivors.
Results: There was a significant effect of ADL balance training on functional balance $F(2.473,51.933)=19.275$, $p=0.000$. The mean functional balance score also increased significantly after ADL balance training [Pre=6.36 ± 3.110, Post=9.36 ± 2.479, $t(21)=-5.41$, $p=0.000$]. The level of significant was set at $p<0.005$.
Conclusion: The results of this study showed that ADL balance training can improve the functional balance in stroke patients. Perhaps, increase in frequency of training would improve the outcome in terms of functional balance performance level.

Keywords: Stroke, functional balance, ADL balance training, unilateral hemiparesis.

FR013

Chlorella vulgaris Supplementation Improves Muscle Strength and Functions of Old Sprague Dawley Rats

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Background: *Chlorella vulgaris* is a coccoid green algal that contains highly nutritious substances with its potential use in pharmaceutical. The aim of this study was to determine the effects of *C. vulgaris* in improving muscle strength and function of old Sprague Dawley (SD) rats and thus combating sarcopenia.
Methods: Thirty SD rats aged 21 months old were divided into three groups; Group 1 (untreated control) was given distilled water, Group 2 was treated with 150 mg/kg body weight (BW) of *C. vulgaris*, and Group 3 was treated with 300 mg/kg BW of *C. vulgaris*. Treatment with *C. vulgaris* was carried out based on the current BW of each rat by oral gavage for three months. At day 30, 60 and 90, several parameters were measured which include grip strength (BIO-GS3, BIOSEB), open field test (HVS image), muscle mass and bone density (DEXA). At day 91, all rats were sacrificed.
Results: No significant different in body weight and relative organ weight for each groups was observed. The grip strength of front and hind paws of *C. vulgaris*-treated rats was significantly increased on day 30, day 60 and day 90 compared to day 0 before the rats were treated with *C. vulgaris*. A similar increase in grip strength of front and hind paws was observed in *C. vulgaris*-treated rats on day 30, day 60 and day 90 compared to untreated control on the same respective days ($p<0.05$). For open field test, total path was significantly increased for rats treated with 300 mg/kg BW of *C. vulgaris* at day 60 and day 90 compared to day 0. However, there was no significant difference between *C. vulgaris*-treated and untreated rats on day 30, day 60 and day 90. The percentage of time moving however did not show any significant difference between *C. vulgaris*-treated and untreated rats. Bone mineral content (BMC), bone mineral density (BMD) and lean BMC of *C. vulgaris*-treated rats was significantly increased on day 30, day 60 and day 90 compared to day 0 ($p<0.05$). There were no significant differences in BMC and BMD between *C. vulgaris*-treated and untreated rats on day 30, day 60 and day 90. Despite that, there was a significant increase of lean BMC in rats treated with 300 mg/kg BW of *C. vulgaris* compared to untreated rats on day 30 and day 60. Additionally, the

percentage of fat mass significantly decreased in 150 and 300 mg/kg BW of *C. vulgaris* at Day 90 compared to untreated control.

Conclusion: Our findings demonstrated that *C. vulgaris* has the capability of promoting muscle regeneration in old SD rats as indicated by improvement in muscle strength and functions. This may further indicate its positive role in the prevention of sarcopenia.

Keywords: *Chlorella vulgaris*, Sprague Dawley rats, muscle regeneration, muscle strength, muscle function.

FR014

Effect of Exercise Training on Hemiparetic Gait of Stroke Survivors: Improving the Step Length Symmetry

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Background: Hemiparetic gait is one of the attributes of post-stroke impairments that interferes with functional and locomotion performance in stroke survivors with hemiparesis. Their step length between paretic and non-paretic lower extremities is typically uneven due to such asymmetrical nature of hemiparetic gait. This research was conducted to evaluate the effect of exercise training on step length symmetry of stroke survivors.

Methods: Seven subjects (4 males, 3 females) with mean age of 48±12.843 were recruited to perform 12-week exercise training that involved paretic lower extremity strength training and treadmill training. Step length was analysedby using Noraxon's myoRESEARCH 3.10.30 software using myoPRESSURE module. The step length was analysed statistically using one-way repeated measures ANOVA (rANOVA) and paired t-test.

Results: The results for ANOVA and paired t-test showed that there were significant effect of 12-week exercise training on step length symmetry ($F(2, 12) = 5.153$, $p = .024$) and ($t = -2.663$, $p=.037$) respectively.

Conclusion: The designed 12-week exercise training had shown statistically significant effect to improve the evenness between their right and left step length.

Keywords: Hemiparetic gait, step length, exercise training, lower extremity.

P001

Modulation of Collagen Type I by Stingless Bee Honey in Cellular Ageing Model

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Background: Naturally-present antioxidants in the skin have an ability to protect the skin from reactive oxygen species (ROS). Cells counteract the ROS attack by activating the antioxidant defence system. However, these defences can be overrun when the amount of ROS is increased. Honey is essential for both nutritional and medical purposes. Stingless bee honey has great medicinal value with proven antioxidant activity. Therefore, our study aims to determine the anti-ageing potential of stingless bee honey in modulating skin ageing of human fibroblasts cells.
Methods: Serial passaging was done and the number of population doublings (PDs) was monitored until fibroblast cells reached senescence (passage 24). At passage 24, fibroblast cells were treated with stingless bee honey and subsequently total RNA was extracted for gene expression analysis. Optimum dose and incubation time of stingless bee honey were determined using MTS assay while the collagen type I expression were analysed using real time RT-PCR technique.
Results: The optimum dose and incubation time of stingless bee honey on cell proliferation of fibroblast cells were 0.02% for 72 hours. Meanwhile, gene expression analysis showed upregulation of the collagen type I in honey treated senescent cells.
Conclusion: In conclusion, this study proposed that stingless bee honey promotes collagen synthesis by modulating collagen type I expression.

Keywords: Stingless bee honey, Collagen type I, Cellular Ageing

P002

Selenium Supplementation Changes Thioredoxin Reductase activity, Telomerase Activity and Telomere Length in Alcohol-Induced Rat Liver

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Backgrounds: Alcohol can induce oxidative stress in human and underlie numerous chronic degenerative diseases. Selenium is a trace element that is needed in small quantities and excessive consumption of selenium just cause toxic effects. one of the selenoproteins that function as antioxidants is the thioredoxin reductase (TrxR) enzyme. This reseach was conducted to get information about how does alcohol-induced oxidative stress and selenium excessive suplementation affect the TrxR activity and mRNA expression that associated with the aging process shown by telomere length and telomerase activity.

Methods: Young male Spague-Dawley rats were randomized into six groups (n=4): control (C), selenium I (Se I), Selenium II, Alcohol (A), Selenium I + Alcohol (Se I + Alc), and Selenium II + Alcohol (Se II + Alc). Ethanol was diluted until concentration 10% as drinking water in alcohol groups and selenium supplemented diets contain additional selenium 0,87 mg/kg for Se I group and 2,03 mg/kg for Se II group. We measure the TrxR mRNA expression and activites, telomerase activities, and telomere length. Supplementation of selenomethionin with or without alcohol-induced decrease TrxR and telomerase activity, increase TrxR mRNA expression and rescues telomere length.

Conclusion: Alcohol administration accompanied by excessive selenium administration may lead to increased expression of TrxR mRNA but this enzyme activity actually decreases. While at telomere, there is an increase in telomere length despite a decrease in teomerase activity which is probably due to the occurrence of ALT.

Keywords: Selenium, stress oxidative, Telomerase and telomere, alcohol-induced rat.

P003

Regulation of Atherosclerosis-Related Genes in Healthy and Diseased Coronary Artery Tissues

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Background: Coronary artery disease (CAD) is the commonest form of heart disease resulted from atherosclerosis, a process which plaque build-up in the inner walls of arteries. Atherosclerosis is a complex and multifactorial disorder, which involves multiple genetic influences and environmental interactions. The disease appear to be influenced by many genes, either with a relatively small effect or in a combination over many years. 11 candidate genes have been predetermined based on the location of genes within regions of interest and prior knowledge of their function. Regulation pattern and polymorphism of candidate genes have been suggested to alter the microenvironment for the disease progression. Details understanding of the susceptibility genes and their genotypic variants is important to generate genomic patient's phenotype for better prevention of disease progression.
Methods: The study involved assessment of differential expression and polymorphism analysis of candidate genes in atherosclerotic coronary artery tissue (ACAT) versus non-atherosclerotic coronary artery tissue (NCAT) samples. Tissues were analyzed through microscopic examination to confirm the healthy and atheroma tissues. Next, RNA was extracted and further analyzed using GeXP genetic analysis system to map out the expression of candidate genes. Restriction fragment length polymorphism (RFLP) analysis were then conducted to investigate the genotypes variation in both sample groups. Descriptive statistics were used to determine genotypes distribution of each polymorphism in both groups and identify the risk association.
Results: Presence of atheroma through morphology finding has confirmed and validated our ACAT samples from NCAT. Our findings indicated that 3 candidate genes (*LDLR*, *TP53*, and *MMP9*) showed significant differences of expression when compared between ACAT and NCAT samples ($p<0.05$). Further RFLP analysis on these genes revealed significant increment in CT genotype and T allele of MMP9-1562C>T polymorphism in ACAT compared to NCAT. There were also positive

associations of CT genotype and T allele with atherosclerosis.
Conclusion: There are significant differences in the expression of *LDLR*, *TP53*, and *MMP9* genes in coronary artery tissues samples. However, genotype variation were only identified in CT genotype and the T allele of the *MMP9*-1562C>T polymorphism. This result also displayed that there were positive associations of CT genotype and the T allele of MMP9-1562C>T polymorphism with the risk of developing atherosclerosis.

Keywords: Atherosclerosis, *MMP9* gene, Restriction fragment length polymorphism (RFLP).

P004

Relationship of Exposure to Cigarette Smoke against the Melatonin Hormone Levels in Rats (*Rattus norvegicus*) Wistar Strain

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Background: Smoking is a common habit that are known to increase the risk of serious health problems related to the respiratory system, cardiovascular system, reproduction, and more. Passive smokers have the same risk of active smokers due to exposure to free radicals on smoking. Melatonin has a very high antioxidant activity. Such activity can neutralize free radicals contained in cigarettes. There is a suspicion of people who smoke have lower melatonin levels in their body. The purpose of this research is to know the relationship of exposure to cigarette smoke against the melatonin hormone levels in rats.
Methods: This research was conducted with methods of experimental research using quantitative data obtained by measurement of absorbance measurement of melatonin levels on rat blood sample. Data analyzed with paired sample T-test using IBM SPSS Statistics 21 for windows.
Results: The results showed levels of the hormone melatonin in the control group of 14 days and 28 days are 0,537±0,103 and 0,695±0,176; while the group's treatment 14 days and 28 days were 0,499±0,161 and 0,479±0,073. P value group of 14 days is 0,441; a group of 28 days was 0,082; and group treatment 0.325 ($p>0,05$).
Conclusion: There is a decrease in the hormone melatonin levels along with the length of the giving exposure to cigarette smoke, but based on statistical tests there was no meaningful difference in hormone levels of melatonin on mice exposed to and do not exposure to cigarette smoke.

Keywords: Smoking, melatonin, rat

P005

A Rapid Sample Preparation for Analysis of Protein *N*-Glycosylation by Mass Spectrometry: Application to Human Serum

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Introduction: Protein glycosylation to produce a normal glycoprotein structure requires the biosynthetic addition and trimming of monosaccharide building blocks by enzymes located in the endoplasmic reticulum and the Golgi apparatus of the cell. The trimming and modification of these oligosaccharides must be in sequence to produce a normal glycan structures. The changes in glycan structures have been associated with one of the Inborn Errors of Metabolism known as congenital disorders of glycosylation. Mass spectrometry is a well established approach for studying glycoprotein glycans. This is due to the small amount of sample required and the possibility of high-throughput analyses of complex mixtures. Here we describe a simple approach for protein extraction from human serum and release of *N*-glycans to simultaneously characterize *N*-glycan profiles.
Objective: To develop a simple, mass spectrometry compatible, filter-aided protocol for the release of glycoprotein *N*-glycans from human serum.
Methods: A method to assess the diversity of the *N*-linked glycans released from human serum has been developed using FANGS protocol. 20 uL human serum are boiled in sodium dodecyl sulfate (SDS), as in the recently-described FANGS protocol the SDS is exchanged for urea, and then for volatile buffer, in which *N*-glycans release using PNGase F is carried out in the upper chamber of a membrane spin filter. The released glycans are recovered in the filtrate following centrifugation.
Results: Standard glycoprotein are used to assess sample processing protocol together with human serum. Non-derivatised *N*-glycans from standard glycoprotein and human serum were analysed using MALDI TOF/TOF MS. Bi and tri-antennary sialylated glycans are observed from standard fetuin for validation of sample processing.
Conclusion: We have developed a simple approach for protein extraction, release of *N*-glycans from human serum in order to study protein *N*-glycosylation.

Keywords: Mass spectrometry, *N*-glycosylation, serum, protein.

P006

Mitochondrial Staining with Mitotracker Dye and Co-localization of Mitochondrial Membrane in Primary Skin Fibroblasts

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Introduction: Mitochondria are highly dynamic organelles with unique morphology and behavior under different cellular stress conditions. Staining with Mitotracker dyes have previously been used for visualization of mitochondria in live cells with good retention after fixation to allow long-term analysis. The focus of our study was to develop a protocol to standardize the concentration and incubation time of Mitotracker Red CMXRos dye to visualize mitochondria in primary skin fibroblasts using wide-field immunofluorescence microscopy. We also developed a protocol for co-staining of mitochondria with mitochondrial outer membrane specific marker TOMM20.

Methods: 5000 primary skin fibroblasts (ATCC) were seeded onto sterilized coverslips in 6 well plates and allowed to adhere overnight. Mitotracker Red CMXRos dye was solubilized in complete media, added to plated cells and incubated at 37°C. Cells were fixed in 3.7% paraformaldehyde before permeablization with 0.1% triton-X and blocking in 1% BSA solution. For mitochondrial membrane co-staining, coverslips were incubated with TOMM20 primary antibody at 4°C in a humidified chamber overnight. Coverslips were incubated in secondary antibody (Alexa Fluor 488) for 1 hour at room temperature before applying DAPI staining for nuclei visualization. Coverslips were mounted on glass slides and imaged using Nikon TiE fluorescence microscope.

Results: Mitotracker Red CMXRos was used at 100 to 500 nM and incubated at 37°C between 30 to 60 minutes. Mitochondrial staining with Mitotracker Red CMXRos was optimized at 100 nM solubilized in complete media with an incubation period of 60 minutes. TOMM20 antibody was used at a 1 µL/mL and secondary antibody at 4 µL/mL.

Conclusion: We have developed a protocol for visualization of mitochondria in primary skin fibroblast through immunoflourescence microscopy by co-staining with Mitotracker Red CMXRos dye and mitochondria outer membrane specific TOMM20 marker.

P007

Effect of Repeated Exposure of Paraquat in the Rats' Piriform Cortex and the Protective Role of Tualang Honey: A Preliminary Finding

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Background: The effects of paraquat in piriform cortex is relatively unknown as compared to its well-known selective nigrostriatal dopaminergic neuronal damaging effect. This study aims to investigate the effect of four weekly exposure to paraquat on rat's piriform cortex and the possible protective effect by Tualang honey.
Methods: Male Sprague Dawley rats were randomly divided into five groups of three animals each. The rats were orally treated with distilled water (2 mL/kg/day; Groups A & C), Tualang honey (1.0 g/kg/day; Groups B & D) and ubiquinol (0.2 g/kg/day; Group E) throughout the experiment period. Two weeks after the respective treatment, the rats were then administered with saline (1 mL/kg/week; Group A & B) or paraquat (10 mg/kg/week; Groups C, D & E) via intraperitoneal injection, once a week for four consecutive weeks. All rats were sacrificed a week after the last injection of saline or paraquat. The perfusion-fixed brains were collected, processed and subjected to cresyl-violet staining.
Results: The present study showed that four weekly exposure to paraquat (Group C) decreases the number of viable cells in the piriform cortex as compared to the control groups (Groups A & B). Pre-treatment with Tualang honey (Group D) or ubiquinol (Group E) increased the number of viable cells in this region when compared to Group C.
Conclusion: The preliminary findings suggest that repeated exposure to paraquat resulted in neuronal damage to the piriform cortex. Treatment with Tualang honey or ubiquinol may have protective effects against paraquat-induced neuronal damage.

Keywords: Paraquat, piriform cortex, Tualang honey

P008

Profiling of Selected Phytoconsituents as Potential Anti-Aging Active Ingredient for Cosmeceutical Preparation

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Background: Skin aging is due to decline of cell tissue functions, proteolytic degradation of fiber network caused visible sign of aging. The use of natural compounds in skin protection especially topical application of phytoconsituents indicates their popularity in decreasing the effect of aging signs on the skin. The phytoconstituents are part of the physiological functions of living plant and hence they are believed to have better compatibility with human body with less adverse effects to health. Phytocontituents originally obtained from plant sources, has been reported to possess various biological properties. Although several studies have demonstrated the anti-oxidative activity of phytoconsituents, its anti-aging profiles has not been established.
Methods: The selected phytoconsituents were observed for antioxidant via DPPH free radical scavenging and superoxide scavenging whereas anti-aging activity via hyaluronidase and anti-elastase inhibitory assay systems.
Results: Quercetin has high activities in all four pathways among the tested phytoconsituents. It showed free radical scavenging, superoxide scavenging and hyaluronidase activity above 85% whereas elastase inhibitory activity was greater than 55%.
Conclusion: The present results demonstrated that quercetin has good potential as free radical scavenger and ability to moist and restore skin elasticity. Thus, quercetin is recommended as an active ingredient for cosmetic product development.

Keywords: Skin aging, antioxidants, phytoconsituents.

P009

Concentrations of Reactive Oxygen Species (ROS) and Malondialdehyde (MDA) in Leukocyte Cells of Hepatitis Patients

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Background: Hepatitis has become a health problem in the world. Indonesia is a country with a high prevalence of hepatitis B with high endemicity. Hepatitis is a disease that attacks the organs that make the liver function, which is where the filtering of toxins in the blood, becomes disturbed. Liver tissue damage can be caused by oxidative stress that binds to free radicals. The presence of liver damage is characterized by increased malondialdehyde (MDA). The purpose of research is to know the concentration of ROS and MDA in leucocyte cells of hepatitis patients.
Methods: The research method is descriptive with case control study, blood sample taken from hepatitis patient from Clinic Pratama Prof. Qomariyah amounted to 31 people including 6 men and 25 women. As a control is a employee of YARSI University, amounting to 31 people including 6 men and 25 women. Measurement of MDA and ROS (isoprostane) using ELISA method with wavelength 450 nm.
Results: The results showed that the concentration of ROS (isoprostan) in the hepatitis group was 20.400 ± 7.4063 pg/mL in males and by 23.471 ± 23.3545 pg/mL in women. While the control group were respectively 11,185 ± 6,4102 pg/mL and 8,350 ± 6,808 pg/mL. MDA concentrations for hepatitis patients were 2.2803 ± 0.3843 µmol/L and 2.3784 ± 0.70 µmol/L in males and females respectively, while in the control group were 1.2452 ± 0.2350 µmol/L and 0.9800 ± 0.1542 µmol/L.
Conclusion: It was concluded that hepatitis patients had higher concentrations of ROS and MDA than healthy people

Keywords: Hepatitis, ELISA, ROS, MDA, leucocyte

P010

The Influences of Sleep Deprivation and Physical Activity towards on the Risk Factors of Degenerative Diseases

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Background: Sleep is one activity for humans to rest the body. Several studies have shown that sleep deprivation (SD) is associated with degenerative diseases such as obesity, incidence of type 2 diabetes mellitus and cardiovascular disease (CDV). Sleep deprivation can decrease energy metabolism resulting in decreased leptin and increased adipocyte cell inflammation which is a risk factor for Obesity. The occurrence of Obesity affect the value of Body Mass Index (BMI) and Waist Circumference (WC). In addition, SD may cause an increase in central nervous system (CNS) which may lead to increased insulin resistance and decreased insulin sensitivity so that insulin can not function properly circulating blood sugar (BS) causing an increase BS in circulating . And increase of Blood Pressure (BP) which is a risk factor for CDV. Physical activity (PA) can increase energy metabolism so as to prevent risk factors for degenerative diseases.
Methods: This research used pre and post test control trial for 6 weeks aimed to know the effect of SD and quantity of PA on risk factor of degenerative diseases such as BMI, WC, BS, and BP value. A total of 60 students of Medical Faculty University Yarsi, consisting of 30 peoples SD chronicles and good activity (To campus on foot) and 30 peoples SD Chronicles less activity (using the vehicle to campus). Measurements of variables BMI, WC and BS are done in the morning as much as 2 times the measurements (week 2 and week 5).
Results: Subjects with Good physical activity got the difference value (delta) for BMI ie 3.14, WC value: 1.9, and BS value: 1.03. In the subject of physical activity less obtained BMI value, WC and BS respectively: -0.15, and 0.33, and 5.97. On Subjects enough physical activity, BP: -1.367 mmHg (systolic), -1.80 mmHg (diastolic). Subjects less physical activity BP: -0.96 mmHg (systolic), -2.23 mmHg (diastolic).
Conclusion: After 6 weeks, the difference in the value of WC, BS and BP (degenerative disease risk factors) was greater in subjects with good physical activity. It shows that physical activity has a positive effect on SD effects.

Keywords: Sleep Deprivation, Degenerative diseases, Waist Circumference, Blood Pressure, physical activity.

P011

Effects of *Piper sarmentosum* Leaf Extract towards Antioxidation and Collagenase Activities

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Background: *Piper sarmentosum* is a fast growing plant known as wild betel that mostly found in Southeast Asia. It was used traditionally to treat malaria fever, cough, and dermatitis. Its leaf extract has been found to possess anti-bacterial and anti-inflammatory activities and it contained various phytochemicals such as polyphenols and flavonoids. However, its anti-collagenase activity is yet to be explored. Hence, total flavonoid content (TFC), the binding affinity and the inhibitory mode of collagenase were examined in this study to envisage the effect of *P. sarmentosum* leaf extract towards collagenase's activity.
Methods: The leaf extract of *P. sarmentosum* was prepared at 1:5 weight per volume ratio using sterilized water. Total flavonoid content (TFC) of crude leaf extract was determined using aluminium chloride method and spectrometric measurement at 510 nm. Standard quercetin (QU) was used as a control and TFC was expressed as mg QU equivalents (QUE) per gram of leaf. The DPPH scavenging activity was conducted to measure the anti-oxidation activity of *P. sarmentosum* leaf extract. The binding affinity of collagenase was assessed using either one-substrate or multiple-substrate reactions and Lineweaver-Burk (LB) plots were generated to determine the K_m for each substrate used. The inhibitory mode of collagenase was examined based on the comparison of the K_m values.
Results: TFC in leaf extract was measured to be 52.0 $\pm$ 0.79 mg QUE per gram of leaf tissues. The scavenging activities of leaf extract and QU were 49.4% and 65.4% respectively. Based on LB plot, K_m for leaf extract was 0.25 mM compared to QU (0.14 mM) and gelatin (0.50mM). The lower K_m indicated better binding affinity towards the active site of collagenase. Hence, both QU and leaf extract were more preferred substrates for collagenase than gelatin. Further analysis indicated competitive mode of inhibition was exhibited by leaf extract when it directly competed with gelatin for the active site of collagenase.
Conclusion: *P. sarmentosum* leaf extract showed high antioxidation via DPPH assay. It served as the preferred substrate by competing with gelatin for the active site of collagenase.

Keywords: *Piper sarmentosum*, collagenase, total flavonoid content, Lineweaver-Burk plot.

P012

GSK-3 Inhibitor Promotes Anti-Inflammatory Responses in LPS-Activated Microglia

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Background: In many neurological conditions, neuroinflammation emerges as a central process that is activated by several cues, including infection and traumatic brain injury. Microglia, a resident macrophage of the brain, is responsible for responding towards these cues. Association of microglial activation with neuroinflammation is characterized by secretion of various neurotoxic mediators such as pro-inflammatory cytokines and nitric oxide. Glycogen Synthase Kinase-3 (GSK-3) is a crucial protein kinase for cell biological function, promotes inflammatory response through its signalling. Previously, the presence of GSK-3 inhibitor in the activated microglia was found to downregulate the pro-inflammatory mediators and upregulate the anti-inflammatory cytokine, IL-10, expression. In this study, we aim to evaluate the efficacy of selected GSK-3 inhibitors in dampening the pro-inflammatory mediators and the gene expression of the associated genes.
Methods: The levels of nitric oxide (NO), inducible nitric oxide synthase (*iNOS*), *TNF-α and IL-6* gene expression and secretion of pro- and anti-inflammatory cytokines in lipopolysaccharides (LPS)-stimulated microglia cell lines, BV2, treated with LiCl or NP12 were determined by Griess assay, qRT-PCR and cytokine bead array, respectively.
Results: Our data shows that inhibition of GSK-3 in the LPS-stimulated BV-2 cells reduced the production of NO and the expression of its associated gene, iNOS. Secretion of pro-inflammatory cytokines including TNF-α and IL-6 was also reduced in the same treatment. In addition, the expression of microglial activation marker, CD11b, also decreased by inhibition of GSK-3. Interestingly, reduced expression of the pro-inflammatory cytokine genes, *TNF-α* and *IL-6*, were coexisted with upregulation of *IL-10* gene expression.
Conclusion: These results suggest that downregulation of the pro-inflammatory responses via inhibition of GSK-3 is mediated by IL-10 action. Induced IL-10 production via inhibition of GSK-3 signalling has potential immunoregulatory effects by suppressing the pro-inflammatory factors in activated microglia.

Keywords: Microglia, Glycogen Synthase Kinase-3 (GSK-3), IL-10, anti-inflammatory.

P013

Effects of TRF and ATF on Oxidative Stress-Induced Osteoclast Formation *in Vitro*

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Background: Imbalance between the productions of reactive oxygen species (ROS) and antioxidant defense mechanisms leads to oxidative stress. Vitamin E is indeed a lipid-soluble antioxidant act by scavenging ROS, and it is believed to protect against bone loss by inhibiting the formation of osteoclasts, the bone degrading cells. In this study, the effect tocotrienol rich fraction (TRF) and α-tocopherol (ATF), as selected examples of vitamin E, on osteoclast formation (also known as osteoclastostoegenesis) *in vitro* was assessed and the possible underlying mechanism was also studied.

Methods: Peripheral blood mononuclear cells (PBMC) from healthy volunteers were cultured in the presence of 25 ng/mL of macrophage colony-stimulating factor (MCSF) and 50 ng/mL of receptor activator of nuclear factor kappa-B ligand (RANKL) for differentiation into osteoclasts. The cells were exposed to 50 μM hydrogen peroxide (H_2O_2) and the effects of 50 μg/mL ATF and TRF treatment on osteoclast formation were assessed through TRAP staining. The impact of TRF and ATF in modulating oxidative stress-induced osteoclastogenesis was also assessed from the intracellular ROS assay and mRNA expression of an antioxidant enzymes, Nrf2.

Results: Treatment with TRF, but not ATF, significantly reduced H_2O_2-induced osteoclast formation following exposure ($p<0.05$). Significant reduction in intracellular ROS was also found in cells treated with TRF, but not in the ATF-treated and untreated groups. TRF might modulate down intracellular ROS through Nrf2, as increased mRNA expression of Nrf2 was observed at both early and late osteoclastogenesis in the TRF-treated group. Interestingly, the group supplemented with TF had shown contradict results for all parameters measured.

Conclusion: Treatment with TRF, but not ATF, suppressed the osteoclast formation *in vitro* possibly through the reduction of intracellular ROS mediated by increased expression of antioxidant enzyme Nrf2.

Keywords: ROS, osteoclast, vitamin E, bone loss

P014

The Effect of Inulin Extract from Lesser Yam on Pancreatic β Cells Counts and Expression of Insulin in Streptozotocin-induced Diabetic Rats

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Background: Diabetes mellitus (DM) is a metabolic disorder, characterized by chronic hyperglycemia that can destruct pancreatic β cells due to its toxic effect. Lesser Yam is Indonesian local vegetable food which has antidiabetic activity. The aim of this study is to evaluate the effect of inulin extract from Lesser Yam on pancreatic β cell count and expression of insulin in Streptozotocin (STZ)-induced Diabetic Rats.

Methods: Forthy two male Wistar rats, 5 months of age, weighing 180-220 g, were divided into 6 groups which each group consisted of 17 rats. Group I (control group), Group II (DM group), Group III (galvus drug control), Group IV was received inulin extract 100 mg/kg body weight rats, orally during 21 d, Group V was received inulin extract 300 mg/kg body weight rats orally, during 21 d, Group VI was received inulin extract 300 mg/kg body weight on day minus-2, during 30 d. Histopathological and immunohistochemical examination was performed to evaluate pancreatic β cells count and insulin expression, respectively. Differences between groups were evaluated by ANOVA.

Results: Analysis on the 21st and 28th day showed that a significant difference of the number of pancreatic β cells between Group I and Group II, between Group II and Group III, IV, V, VI. On day 14th, the insulin expression of pancreatic β cells between Group I and Group II, Group II with Group III, IV, V and VI was significantly different. There was a significant difference of the insulin expression of pancreatic β cells on the 21st and 28th day treatments between Group I and Group II, between Group II and Group III, IV, V, VI.

Conclusion: Giving of inulin extract from Lesser Yam influenced to increase the cells number and insulin expression of pancreatic β cells in STZ-induced diabetic rats. The administration of inulin dose variation did not have a significant effect on the number and insulin expression of pancreatic β cells of wistar rats.

Keyword: Inulin, pancreatic β-cell, expression of insulin, streptozotocyn.

P015

Effect of Extract Inulin from Lesser Yam (*Dioscorea esculenta*) on Plasma Insulin and Blood Glucose Levels of The Wistar Rats Induced Streptozotozin

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Background: Diabetes mellitus (DM) associated with increased blood glucoa levels. Lesser yam is inulin contain and required to decrease blood glucose level. This study aimed to examine the effect of the extract inulin from Lesser yam (*Dioscorea esculenta*) to plasma insulin and blood glucose levels of induced wistar rats with streptozotocin

Methods: The research method is experimental with pretest posttest design modifications randomized controlled group design. Fourty two wistar divided into 6 groups (Control group I, group II, group III, group IV, group V and group VI). Plasma insulin and blood glucose levels were measured by Spectrophotometer. Data was analyzed by Wilcoxon and Kruskal Wallis test.

Results: The result showed that 1. The effect of antioxidant extract of inulin from lesser yam (*Disocrea esculenta*) is very strong; 2. Extract of inulin effect on plasma insulin levels and blood glucose levels of wistar rats induced by STZ

Conclusion: Inulin from lesser yam (*Dioscorea esculenta*) in SD rats induced by several dose of STZ can increased plasma insulin and reduced blood glucose level.

Keywords: Extract inulin, insulin levels, glucose levels, streptozotocin.

P016

High-throughput Screen for Plant Extracts that Extend the Chronological Life Span of Ageing Yeast *Saccharomyces cerevisiae*

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Background: The model organism budding yeast *Saccharomyces cerevisiae* has been widely studied for the determination of mechanisms and signalling pathways involved in ageing. Chronological life span (CLS) ageing is the study of the mean and maximal survival time of yeast population in a non-dividing state. Most of the discovered ageing pathways from *S. cerevisiae* have been highly conserved in higher eukaryotes especiallymammals and human being. Bioactive compounds are mainly the secondary metabolites produced in different parts of plant that can be extracted as crude or refined plant extracts (PEs). These compounds can elicit pharmacological activities in organisms. Hence, a high-throughput screen of 223 Malaysian plant extracts was performed to determine its anti-ageing activity on chronologically ageing yeast strain BY20119.
Methods: A standard high-throughput method as reported by Murakami *et al.* 2008 was modified to suit our laboratory conditions, to ensure a standard and un-bias measurement of yeast chronological lifespan. The CLS of the ageing yeast was monitored through the outgrowth of the ageing culture. Plant extracts tested on the cells were dissolved in 100% dimethyl sulfoxide (DMSO). The PEs were further tested in a dose-dependent manner and chronic oxidative and thermal stress assays were carried out to exlporethe anti-ageing effects of the PEs.
Results: Of the 223 PEs screened, extracts from *Wodyetia bifurcate*, *Cascabelathevetia* and *Ziziphusmauritiana* had the highest anti-ageing activity on ageing yeast BY20119. These extracts extended the chronological life span of yeast by maintaining the survival rate of the cell population above 60% after eight-ageing days.
Conclusions: Natural compounds with anti-ageing properties can serve as a bio-probe to study the biological process and conserved longevity pathways of ageing in living organisms.

Keywords: Chronological life span, survival, bioactive compounds, anti-ageing.

P017

Antioxidant Activity of Ethanolic Extract of Callus developed from Carrot (*Daucus Carota* L.) and Tomato (*Solanium Lycospericum* L.)

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Background: The accumulation of damaged cells might lead to some degenerative diseases. Antioxidant substances contained in plants have activity to prevent occurrence of the disease. Carrot (*Daucus carota* L.) and tomato (*Solanum lycopersicum* L.) are high potential source of antioxidant compounds such as phenolic and carotenoids. Callus, as plant stem cells developed from carrot and tomato plants might also contain bioactive compounds as antioxidant that can be used to prevent the degenerative diseases. This study was aimed to investigate antioxidant activity of callus extracts developed from carrot and tomato plant organ on Murashige and Skoog medium.
Methods: The medium was varied at sucrose concentration of 30 g L^{-1} and 40 g L^{-1} and at 2,4-D concentrations were 0, 1, 2, 4, and 8 mL L^{-1}. The grown callus was extracted using ethanol and measured on their antioxidants activity using DPPH method. Bioactive contents in the extract were also determinated using chromatography technique.
Results: Antioxidant assay found that IC_{50} of ethanolic extract of carrot callus was 1751.29 $\pm$ 4.00 mg mL^{-1}, while ethanolic extract of tomato callus was 620.56 $\pm$ 32.36 mg mL^{-1}. In contrast, Quercetin as reference standard had IC_{50} value of 2,85 mg mL^{-1}.
Conclusion: According to the result, both ethanolic extracts contained phenolic and terpenoid compounds. The compounds might have a contribution in the antioxidant activity.

Keywords: Antioxidant, callus, carrot, tomato.

P018

The Effects of Oral Glutathione Differential Dosage on Healthy Overweight Volunteers

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Background: Glutathione (GSH) is a natural tripeptide antioxidant that can be found in human body and food supply. Oral supplementation act as a catalyst for the enzymes that synthesize glutathione within the cell to exert antioxidant function thus maintaining the efficacy of glutathione system in the body. This preliminary study aims to observe the effect of supplementation dosage on healthy overweight volunteers with body mass index (BMI) more than 25. The components investigated were plasma GSH value, fasting glucose level, and cholesterols level.
Methods: Volunteers are randomised into 3 groups; Group 1 with one dose of 5g supplement, Group 2 with two doses of 5g at different time which are in period of 8 hours interval (doses taken before breakfast and dinner) and Group 3 with volunteers consuming two doses of 5g at the same time (both dose taken before breakfast). Nine female volunteers were observed in this study.
Results: After four weeks of supplementation, data from the nine volunteers were analysed. The plasma GSH value increases to approximately, 4.36 $\pm$ 1.7 µM, 3.65 $\pm$ 2.5 µM, 3.83 $\pm$ 0.4 µM for Group 1, Group 2 and Group 3, respectively.
Conclusion: Based on the plasma GSH value, Group 1 has the most increment as compared to groups 1 and 2. Positive outcome was also observed in fasting glucose, triglyceride, total cholesterol and low-density lipoprotein (LDL) cholesterol levels. In conclusion, one dose of glutathione supplementation is sufficient to maintain plasma GSH level in the body and thus, may help to improve glucose and cholesterols level in blood.

Keywords: Glutathione, supplementation, dosage.

P019

Antidepressant and Antioxidant Properties of A-Mangostin in Type-2 Diabetic Rats

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Background: The prevalence of depression is approximately 18% higher in diabetic patients and this co-morbid condition is rising at alarming rate in today's population. Chronic diabetes will lead to many complications including depression due to consequences of changes of biochemical. The objective of our research was to evaluate antidepressant activity of α-mangostin via antioxidation activity in diabetic rats.

Methods: The wistar rats in the experimental groups were rendered hyperglycaemic with a single dose of streptozotocin (STZ 55 mg/kg, i.p). All animals were tested for signs of depression using the forced swimming test and tail suspension test models. Four groups were compared: (1) normal group, vehicle treated (2) normoglycemic, α-mangostin treated (3) hyperglycaemic, vehicle treated (4) hyperglycaemic, α-mangostin treated rats for 21 days. On the last day of the study, brain samples were collected to measure the oxidative stress by using the thiobarbituric acid reactive substances (TBARS) assay.

Results: α-mangostin was administered to the STZ-treated rats, this reversed the STZ-induced increase in immobility duration in the forced swimming test (FST) and tail suspension test. Treatment with α-mangostin attenuated STZ induced oxidative species, as indicated by significantly ($p<0.05$) decreased malondialdehyde level in the brain. These results suggest that antidepressants and antioxidants can counter the mood and oxidative disorders associated with diabetes.

Conclusion: In conclusion, we demonstrated that α-mangostin has antidepressant-like properties, probably based on its antioxidant effects, and is thus relevant for the treatment of depression.

Keywords: Depression, diabetes, oxidation, α–mangostin.

P020

Effect of Exposure of Mobile Phone on Response Malondialdehid and Melatonin in Rats (*Rattus norvegicus* L)

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Background: The mobile phone has been helped the field of communication, information and entertainment. However continued use will affect its users. The aim of this study was to measure levels of malondialdehyde (MDA) and melatonin hormones in white rats (*Rattus norvegicus* L) Sprague Dawley strains exposed to electromagnetic waves of mobile phones in light and dark.
Methods: Rats are divided into 3 groups, each group consisting of 10 tails. Group I (control) without treatment. Group II was given exposure to mobile phone waves for 60, 180 and 360 minutes in light.The group III was given exposure to mobile phone waves for 60, 180 and 360 minutes in dark. Analysis of malondialdehyde (MDA) and melatonin hormones was observed by spectrophotometric.
Results: The results showed that MDA levels of rats exposed to mobile phones light for 60, 180 and 360 minutes were 1.94; 2.04 and 2.13 nM higher than control (1.79 nM). MDA levels of the dark were 1.68; 1.65 and 1.59 nM were not significantly different from control (1.78 nM). MDA levels of light rats group were higher than the dark-group of any given cell phone exposure. Furthermore, melatonin levels of rats in light for 60, 180 and 360 minutes were 0.069; 0.048 and 0.032 ng/ml lower than control (0.146 ng/ml). As for the rats exposed to mobile phones in 60, 180 and 360 minutes in the dark were 0.173; 0.069 and 0.037 ng/ml compared to control (0.176 ng/ml).
Conclusion: These data suggest that, the exposure to electromagnetic waves of mobile phone had increased MDA levels also decreased melatonin hormones, may be represent mobile phones can activated oxidative stress and affect of serious health problems of the user.

Keywords: Cellular phone, electromagnetic, melatonin, malondialdehyde, oxidative stress.

P021

Neuroprotective Effects of Xanthone Enriched Fraction of *Garcinia mangostana* (XEFGM) and α-Mangostin (α-M) on Cognitive and Cholinergic Functions in Chronic Cerebral Hypoperfusion Rats

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Background: Xanthone isolated from pericarp of *Garcinia mangostana* has been reported to exhibit neuroprotective effect *in vitro* and *in vivo* due to its potent antioxidative properties. In this study, the effect of Xanthone Enriched Fraction of *Garcinia mangostana* (XEFGM) and its compound α-mangostin (αM) were investigated on cognitive and cholinergic functions in chronic cerebral hypoperfusion rats (CCH).
Methods: Male Sprague Dawley rats weighed 250g-300g were subjected to permanent bilateral common carotid arteries occlusion (PBCCAO) and sham-operated surgery. Two weeks after surgery, CCH rats were orally administered with XEFGM (25, 50 and 100 mg/kg) and α-mangostin (25, 50 mg/kg) prior to locomotor activity and Morris water maze (MWM) tests, respectively. After MWM test, brain tissues in the hippocampus, frontal and remaining cortex were isolated for acetylcholinesterase (AChE) analysis.
Results: The results showed that there is no significant difference between the groups in locomotor activity. However, the administration of M (50 mg/kg) and XEFGM (100 mg/kg) reversed the cognitive impairment induced by PBCCAO in the spatial learning and memory test. In addition, M (50 mg/kg) showed significant improvement in reference memory. Treatment with M (50 mg/kg) also significantly increase the AChE activity compared vehicle treated PBCCAO in hippocampus.
Conclusion: αM ameliorated learning and memory deficits in CCH by reversing AChE activities in hippocampus. Hence, αM may be a promising therapeutic agent for CCH associated neurodegenerative diseases, including vascular dementia and Alzheimer's disease.

Keywords: Chronic cerebral hypoperfusion, locomotor activity, Morris water maze, XEFGM, αM

P022

Stress-Related Gene Expression in Mice Ovary Following Exposure to Exogenous Corticosterone

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Background: Elevated costicosterone (CORT) level during stress has been proposed as one of the mechanism for oxidative damage in female reproductive system. It has been shown that the detrimental effects of corticosterone induced-oxidative DNA damage leads to reduced oocyte and embryo quality, fertilization and implantation failure thus negatively influence reproductive outcome. This study was designed to define the stress-related gene expression in mice ovary following exposure to exogenous CORT thus indicates that oxidative damage in ovary contributes to poor quality of oocytes.
Methods: Six-week-old female mice (*Mus musculus*) were equally divided into two groups; Group 1: vehicle control was given via intraperitoneal injection, Group 2: CORT (10 mg/kg body weight (BW) was administered intraperitoneally for two weeks. At the end of the treatment period, mice were euthanized. The ovaries were collected for total cellular RNA isolation, amplification and microarray hybridization. Microarray analysis was used to determine the stress-related gene expression in mice ovary from the two groups.
Results: Results showed that a total of 36 stress-related genes undergo a greater change in differential expression following CORT exposure with 5 genes were upregulated and 31 genes were down regulated. Overall, the changes indicate a change in metabolic rate, dynamic change in DNA methylation of stress associated genes and oxidative stress response that might negatively influence the oocytes quality.
Conclusion: In summary, this study profiled the gene expression pattern in mice exposed to exogenous CORT, which adds to the understanding of mechanism of CORT-induced oxidative damage in female reproductive system leading to poor oocyte quality.

Keywords: Corticosterone, oxidative stress, ovary, oocyte, female reproductive system.

P023

The Effect of Steamed Tomato on Catalase and Superoxide Dismutase Level in Hypercholesterolemia Rat (*Rattus norvegicus)* Strain *Sprague Dawley*

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Background: Oxidation activity of LDL-cholesterol increases in patients with hypercholesterolemia. Cholesterol oxidation inside endothelium, generates production of reactive oxygen species (ROS). ROS leads to tissue damage thus increasing endogenous antioxidant activity. The steamed tomato extract contains high antioxidants that are able to substitute endogenous antioxidants and scavenging free radicals in the body. This research aimed to describe the effect of steamed tomato extract on production of endogenous antioxidants.
Methods: This study is an experimental research. Total of 24 rats were divided into four groups and threated for 30 days. The control group (K_0) was administrated only olive oil, the treatment group, K_1 was supplemented with tomato extract 4 mg/KgBW/day, K_2 was supplemented with 8 mg/KgBW/day steamed tomato extract, and K_3 was supplemented with 16 mg/KgBW/day of steamed tomato extract. Data on catalase (CAT) and superoxide dismutase (SOD) level were analyzed with ANOVA and continued with LSD tests.
Results: Based on the results, the lowest CAT level is in K_3 there was 2.89 µl/ml and SOD is 21.21%. While in K_0, CAT level was 8.76 µl/ml and SOD was 67.73%. It was decreased significantly different in the treatment group (K_1, K_2, and K_3) compared to the control group (K_0). The antioxidant content of steamed tomatoes prevents the atherosclerosis build up and oxidation of cholesterol in the endothelial wall. It was indicated by decreased endogenous antioxidant status such as CAT and SOD.
Conclusion: So it can be concluded that administrating steamed tomatoes in rats for 30 days, correlated with decreasing CAT and SOD levels.

Keywords: Catalase, hypercholesterolemia, SOD, tomato extract.

P024

Hypoxia Up Regulates Angiotensin Converting Enzyme in the Chronic Hypoxia Rat Lung

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Background: The chronic hypoxia condition induces adaptation responses to defend homeostasis in the body. Physiology responses such as increase heart pulse and respiratory rate were example of responses to increase oxygen supply in order to assure various organs have sufficient oxygen. HIF-1α, a transcription factor regulates many of genes to work in such condition. The lung is organ that produces angiotensin converting enzyme (ACE) which conver angiotensin I to angiotensin II through renin angiotensin aldosteron system (RAAS). The mechanism increase blood pressure for save the organs from damage because of insufficient oxygen. This study aimed to analyze responce of HIF-1α, and ACE in the rat lung chroniccally hypoxia.
Methods: Male Sprague Dawley rats (n-25) were exposed to chronic systemic hypoxia (O_2 10%; N_2 90%) 1,3,5 and 7 days. mRNA expression of HIF-1α was analyze using real time RT-PCR, HIF-1α protein was determined with ELISA method. Activity of ACE I was analyze spectrophotometrically.
Results: mRNA expression of HIF-1α increased in 5 days (p=0,006), and HIF-1α protein found highest at days 7 after induction (P-003) consecutively. Both was found correlate significantly. Eventhough expression of ACE I increased during induction (in other determination), but activity of ACE I was found stay. Strong correlation was found between expressions of HIF-1α and ACE I.
Conclusion: Chronic hypoxia condition incresed expression of HIF-1α, HIF-1α protein and ACE I enzyme, while activity of ACE I was stay. This result show that hypoxia up regulate angiotensin converting enzyme (ACE), while activity of this enzyme possibly activated with other regulation.

Keywords: Chronic hypoxia, angiotensin converting enzyme.

P025

Anti-Inflammatory Potential and Antioxidant Activity of 'Ya-Samarn-Phlae' a Thai Traditional Herbal Remedy for Wound Treatment

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Background: Thai traditional healers regularly use medicinal plant formulas for healing diseases, but there are few studies to support their claims. This present study was carried out to investigate the anti-inflammatory and antioxidant properties of Ya-Samarn-Phlae (YaSP), a Thai traditional herbal formula, which has been used in patients with diabetic foot ulcers.
Methods: Ethanol and methanol extracts of YaSP were evaluated for their antioxidant activity of using DPPH and ABTS assays. Total contents of phenolics and flavonoids of the extracts were additionally examined. The ethanol extract were further tested for its anti-inflammatory activity in LPS stimulated RAW 264.7 cells.
Results: The extracts exerted moderate DPPH and ABTS radical scavenging ability about 10-30% at concentration of 1.5 µg/mL. Their contents of phenolics and flavonoids were found to be approximately 100 mg gallic acid per g extract and 0.1 mg catechin per g extract, respectively. Moreover, the ethanol extract significantly reduced the nitric oxide production in LPS stimulated RAW 264.7 cells at concentrations of 10-20 µg/mL.
Conclusion: Based on results observed in this study, YaSP should be recorded as an herbal remedy used for wound treatment which possessed moderate antioxidant activity and exhibited notable anti-inflammatory activity. The results provide promising evidence for the potential application of YaSP in diabetic foot ulcer management.

Keywords: Antioxidant activities, Anti-inflammatory activity, traditional polyherbal formula, Ya-Samarn-Phlae, wound healing.

P026

In vitro Antioxidant Activities of Two Traditional Herbal Mixtures Described in Thailand National List of Essential Medicines (Herbal Medicines)

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Background: Oxidative stress has been a major cause of global disease burden. In Thai traditional medicine, polyherbal mixtures have been used as key components of the treatment. This study was aimed at investigating the antioxidant capacity of Ya-Tri-Phigut (YTP) and Ya-Tri-Karsomas (YTK) used as health rejuvenating tonic recorded in National List of Essential Medicines (Herbal Medicines) in Thailand.
Methods: Aqueous extracts of the two formulations were examined for their bioactive constituents through their total phenolic contents (TPC) and their total flavonoid contents (TFC). In addition, their antioxidant capacities were evaluated through a series of chain-breaking and preventive antioxidant assays.
Results: From the *in vitro* analyses carried out, the YTP formulation possessed good free radical scavenging ability as revealed by the DPPH and ABTS radicals scavenging assays with $IC_{50} \pm$ SD values of 0.25 $\pm$ 0.00 mg/ml and 0.20 $\pm$ 0.00 mg/ml respectively. The superoxide radical inhibitory activity of YTP was better with an $IC_{50} \pm$ SD value of 0.02 $\pm$ 0.00mg/ml when compared to that of YTK with 0.28 $\pm$ 0.012 mg/ml. In a similar fashion, the metal chelating activity and FRAP value of YTP were better than those of YTK formulation. However, YTK showed higher bioactive contents compared to those revealed by the YTP formulation.
Conclusion: Therefore, Ya-Tri-Phigut showed a promising antioxidant activities and it could be an important pharmaceutical and nutraceutical remedy against oxidative stress related degenerative diseases.

Keywords: Antioxidant activities, traditional polyherbal formula, herbal remedy, National List of Essential Medicines.

P027

Administration of Jackfruit (*Arthocarpus Heterophilus*) Tree Bark Extract Cream Prevents the Increase of Melanin Amount in Guinea Pig (*Cavia Porcelus)* Exposed by UV-B Ray

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Background: Jackfruit (*Artocarpus Heterophillus)* tree bark ethanol extract contains antioxidant, phenolic, *tannin,* steroid, linoleic acid ethyl ester *and also vitamin C,* it can inhibit the increase of melanin amount in melanocyte while hydroquinone is used as the gold standard for hyperpigmentation treatment until now. This research aimed to study whether the administration of jackfruit tree bark extract cream can inhibit the increase of melanin amount in guinea pig exposed by UV-B ray and compared the effectivity of jackfruit tree bark extract cream 4% with hydroquinone cream 4%.

Methods: This study was an experimental laboratory research by using randomized post test only group design. The independent variable is the jackfruit tree bark extract cream dose and the hydroquinone cream, while the dependent variable is the melanin amount in epidermal layer. A total of thirty guinea pigs (*Cavia Porcelus*) used in this study were split into 3 groups consisted of 10 male guinea pigs in each group, which were one treatment control group administered with basic materials cream and two treatment administered with hydroquinone cream 4% and jackfruit tree bark extract cream 4%. All of the treatment group were exposed by UV-B ray with total dose of 390 mJ/cm^2 for 2 weeks, and then biopsy was undergone to examine melanin amount in epidermal layer. One way ANOVA was used to analyze difference between control group and treatment group 1 and 2 and continued with Least significant Difference (LSD) was used to analyze the existence of treatment difference after treatement ($p<0,05$).

Results: Result of the study showed that melanin amount of the group control was 54.33 $\pm$ 4.52% Significant decrease in the mean of melanin amount in treatment group 1 was 3.01 $\pm$ 0.89% In treatment group 2 there was 4.23 $\pm$ 1.82% of melanin amount. The difference between control group and treatment group 1 and 2 was

significant in decreasing the melanin amount in epidermal layer ($p<0,05$). In the treatment group 1 and 2 was not significant in decreasing the melanin amount in epidermal layer ($p>0,05$).

Conclusion: The conclusion of this study was that 4% jackfruit tree bark ethanol extract cream could decreased melanin amount in epidermal layer. Administration of 4% jackfruit tree bark ethanol extract cream had the same effectiveness with 4% hydroquinone cream prevented the increase of skin melanin in guinea pig.

Keywords: Jackfruit tree bark extract cream, melanin amount, UV-B ray.

P028

Evaluation the Antioxidant Activity of Aromatherapy Massage Oil Prepared from Thai Traditional Wisdom

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Background: The use of aromatherapy as an alternative and complimentary therapy are well-established worldwide. Aromatherapy massage oils, which contain of carrier oils and essential oils, is one of the products commercially available. This study therefore aimed to evaluate antioxidant activity of four types of carrier oils which made according to Thai traditional wisdom.
Methods: The carrier oils (CS-MS-001, CS-MS-002, CS-MS-003, and CS-MS-004) were prepared by mixing some local medicinal plants with coconut oil, rice bran oil or black seed oil. Antioxidant activities of extracts obtained from each oil were done by DPPH and ABTS assays.
Results: In the DPPH method, CS-MS-003 extract demonstrated the most potent antioxidant properties (IC_{50} 0.395±0.02 mg/ml), while CS-MS-001, CS-MS-002, CS-MS-004, and Trolox had IC_{50} of 0.957±0.01, 9.050±1.3, 2.050±0.06 mg/ml, and 0.81±0.06 mM, respectively. Even though, results obtained from the ABTS radical scavenging assay slightly provide some correlation with the DPPH assay. It should be noted that CS-MS-001 extract exhibited the most potent antioxidant properties (IC_{50} 2.28±0.15 mg/ml), while CS-MS-002, CS-MS-003, CS-MS-004, and Trolox had IC_{50} of 11.72±0.12, 2.60±0.29, 5.49±1.34, and 2.82 ±0.12 mM, respectively.
Conclusion: The tested carrier oils, CS-MS-001 and CS-MS-003 possessed notable antioxidant activities, therefore these oils can be used to generate an appropriate aromatherapy massage oil and should be further determine on their effectiveness and safety of these antioxidant oils.

Keywords: Antioxidant activities, Traditional polyherbal formula, Massage oil, Aromatherapy, Traditional Thai medicine

P029

Antioxidant Properties of a Traditional Polyherbal Rejuvenating Formula 'Phy-Blica-O' and its Microencapsules

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Background: Plant-derived compounds such as phenolics, flavonoids, and phenolic acids are an important group of active natural antioxidants, which can be developed as functional ingredients to delay the oxidation of protein, lipid, and DNA. Antioxidants can delay or inhibit the initiation or propagation of oxidative chain reactions. This study was aimed to explore the antioxidant capacity of Phy-Blica-O extract as well as its microencapsules.
Methods: The water extract of Phy-Blica-O was microencapsulated by spray drying in various ratios of gum arabic and maltodextrin as wall materials. The original and encapsulated Phy-Blica-O extract were tested for their total phenolic content and antioxidant activity by DPPH, ABTS, metal chelating, and FRAP assays.
Results: Antioxidant analyses carried out revealed that that Phy-Blica-O extract was most active in the DPPH (IC_{50} value 0.18 mg/ml), and ABTS assays (IC_{50} value 0.06 mg/ml). The extract exhibited superoxide anion free radical scavenging capacity with IC_{50} of 0.21 mg/mL. High encapsulation efficiency was obtained for all extract encapsulating microbeads (75.90-94.03%). Produced Phy-Blica-O encapsules using the ratios of maltodextrin: gum Arabic (8:2) and core: wall (1:2) at inlet temperatures of 140 and 180 C obtained the highest yields and showed good antioxidant activity.
Conclusion: The present studies suggest that the developed formulation has potent antioxidant activity and could be used as functional ingredients for food production. Regarding the physicochemical properties and antioxidant activity, the sample produced with maltodextrin: gum Arabic (8:2) showed the best results, with the highest biological activity, as well as the lowest hygroscopicity, being selected as the most appropriate formulation for encapsulation of Phy-Blica-O.

Keywords: Antioxidant activities, traditional polyherbal formula, Phy-Blica-O, Traditional Thai medicine.

P030

Evaluating the Safety and Bioavailability of Tocotrienol-rich Fraction Formulated into Palm Kernel Olein and Palm Oil Carrier in Rats

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Background: Vitamin E particularly tocotrienol isomer has been reported to have low bioavailability in blood plasma which limits its biological activities as compared to α-tocopherol. This study aimed to evaluate the safety and bioavailability of tocotrienol-rich fraction (TRF) formulated into palm kernel oil (PKO) and palm oil (PO) carrier in rats.

Methods: Female Sprague Dawley rats were orally supplemented with vehicle or TRF formulated into palm kernel oil (PKO+TRF) or palm oil (PO+TRF) and further divided into three types of supplementation: (a) unrepeated one dosage and observed for 14 days (acute unrepeated), (b) daily dosage for 14 days (acute repeated) or (c) daily dosage for 90 days (sub-chronic). Blood was collected at day 0, 7 and 14 or day 0, 30, 60 and 90 for liver profile and vitamin E level determination.

Results: Liver profile results showed that acute unrepeated supplementation of PO+TRF increased the level of alanine transaminase (ALT) at day 7 ($p<0.05$). Meanwhile, rats supplemented with PKO+TRF showed increased ALP level at day 7 compared to day 0 ($p<0.05$). For acute repeated supplementation of PO+TRF, our results showed increased globulin level at day 7 ($p<0.05$). The sub-chronic supplementation of PO+TRF caused increased globulin level at day 60 ($p<0.05$) and the supplementation of PKO+TRF increased albumin level at day 90 ($p<0.05$). No sign of toxicity was observed for all types of supplementation. Determination of plasma vitamin E isomer bioavailability in acute unrepeated supplementation of PKO+TRF showed high concentration of α-tocotrienol at day 7 ($p<0.05$). Acute repeated supplementation of PKO+TRF increased all TRF isomers at day 14 significantly ($p<0.05$). Meanwhile sub-chronic supplementation of PO+TRF

increased the level α-tocopherol and α-tocotrienol at day 30 ($p<0.05$) and increased β-tocotrienol, γ-tocotrienol and δ-tocotrienol levels at day 60 and 90 significantly ($p<0.05$). Supplementation of PKO+TRF results in increased γ-tocotrienol level significantly at day 30 ($p<0.05$). In addition, supplementation of PKO+TRF increased the concentration of δ-tocotrienol significantly as compared to supplementation of PKO only and PO+TRF at day 30 ($p<0.05$).

Conclusion: Supplementation of formulated TRF in palm kernel oil or palm oil carrier is safe and palm kernel oil carrier increased the bioavailability of all TRF isomers and α-tocopherol in plasma when supplemented in acute repeated and acute unrepeated dosages.

Keywords: Safety, biological availability, tocotrienol, palm kernel oil, palm oil.

P031

Effect of Astaxanthin on Specific Activity of Glutathione Peroxidase in Liver Tissues after Oral Induction of Formaldehyde in Male Wistar Rat (*Rattus norvegicus*)

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Background: In Indonesia, formaldehyde is an aldehyde which is found illegally used as a food preservative. Formaldehyde can increase free radicals production leading to cause oxidative stress which can damage liver tissues. Antioxidant like astaxanthin is needed to tackle formaldehyde-induced free radicals. Astaxanthin is expected to increase the spesific activity of enzymatic antioxidant, glutathione peroxidase (GPx). This study aims to determine the effect of astaxanthin on specific activity of glutathione peroxidase in liver tissues of oral formaldehyde-induced male wistar rats (*Rattus norvegicus*).
Methods: This study was an experimental study with posttest-only control group design. Thirty rats were divided into 5 groups: normal control group; the negative control group which was given only formaldehyde; Group 1 which was given a 12 mg/day dose of astaxanthin; Group 2 which was given a 24 mg/day dose of astaxanthin; Group 3 which was given 48 mg/day dose of astaxanthin. Samples were tested with specific activity reagents for glutathione peroxidase (GPx). The data were analyzed using Kruskal Wallis followed by Mann-Whitney
Results: Specific activity in the normal control was 108,21 U/mg, negative control was 62,83 U/mg, dose I was 122,48 U/mg, dose II was 152,88 U/mg, dose III was 175,18 U/mg. The dose I group showed higher activity than the control normal group. In the test dose I and II showed activity GPx specific liver tissue were significantly different than the normal control group ($p \leq 0.05$). Levels activity of a specific enzyme dose I doesn't experience a meaningful difference with normal control ($p > 0.05$)
Conclusion: Astaxanthin could act as an antioxidant by increasing spesific activity

of glutathione peroxidase in liver tissue. The best dose contained in the dose group 12 mg/day.

Keywords: Antioxidant, astaxanthin, formaldehyde, spesific activity of glutathione peroxidase, GPx.

P032

A Secretomic Landscape of Human Gut Microbiome in Healthy and Colorectal Cancer-Stricken Gut

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Background: Understanding gut health via host-microbes interaction has emerged as key strategy for early detection of colorectal cancer (CRC). Protein secretions from the human host and microorganisms may play important roles in the pathophysiology of CRC. We aim to identify the secreted proteins released from the human CRC-stricken gut and gut microflora by assessing the secretome in the stool samples of CRC patients and control.
Methods: Stools samples from 26 clinically-diagnosed patients with CRC and 20 non-CRC control individuals were collected, homogenized and filtered followed by protein extraction and profiling by quantitative label-free proteomics using Nano-Liquid Chromatography TripleTOF Mass Spectrometry. The mass spectra datasets were searched using MaxQuant against the *Homo sapiens* and microbial Uniprot Fasta databases. Statistical analyses were performed using Mann-Whitney, Kruskal-Wallis and Spearman correlation with *p*-value less than 0.05.
Results: We have identified a total of 2037 proteins secreted by the human gut with more than half of the proteins were exclusively expressed in the CRC. A distinct secretion profile was observed between CRC and control, as well as early and late stages of CRC. The human gut proteins that were exclusively secreted in the CRC were mapped to tumorigenesis function. Intriguingly, out of the 1160 CRC-associated proteins, we have found two (2) significant human proteins (Huntingtin & RNA exonuclease 5) that were exclusively expressed in Stage IV of CRC ($p<0.05$). On the contrary, we have identified a total of 2132 proteins secreted by the gut flora (1370 from bacteria; 589 from fungi; 112 from archaea; 45 from viruses; 16 from parasites) with 96 proteins specific to CRC. Interesting discriminative distributions of the microflora's secretome proteins in CRC and non-CRC were observed with great individual variation.
Conclusion: Taken together, these proteins could be viewed as promising biomarkers for the diagnosis or prognosis of CRC. To our best of knowledge, we are the first group to report this stool-derived host-microbes network of the gut

microbiome secretomic landscape.

Keywords: Colorectal cancer, gut microbiome, mass spectrometry, proteomics, secretome.

P033

Effect of Rambutan (*Nephelium Lappaceum* L) Peel Extract on the Malondialdehyde Levels in Blood of Rats Exposed to Cigarette Smoke

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Background: Cigarette smoke contains many toxic compounds that potentially become free radicals and lead to the occurrence of oxidative stress. Under oxidative stress conditions, free radicals resulting in lipid peroxidation of cell membranes and damage to the organization of cell membranes. This study aimed to analyze the effect of rambutan (*Nephelium lappaceum* L) peel extracton the level of Malondialdehyde (MDA) in blood of rats exposed to cigarette smoke.
Methods: This study was conducted on 25 White Wistar Rats, divided into 5 groups: K1 (normal), K2 (negative), and K3, K4, and K5 (treated by the administration of rambutan peel extract with the dose of 3, 6, and 12 mg/200 g body weight respectively) for 30 days. The data were analyzed by One Way ANOVA test followed by LSD test.
Results: The result of data analysis showed that there was a significant difference between the levels of MDA in lung and blood of control and treatment group.
Conclusion: In conclusion, this result showed that the most effective dose of rambutan peel extract for declining the MDA levels in blood of rats exposed to cigarette smoke is 3 and 6 mg/200 g body weight respectively.

Keywords: Cigarette smoke, malondialdehyde, rambutan peel extract.

P034

The Effect of Antioxidants on Rambutan Peel Extract on the Amount of Alveolar Macrophage in the Lung Exposed to Cigarette Smoke in the Mouse Model

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Background: Rambutan is one of the many cultivated plants in Indonesia to be utilized by its fruit. Rambutan fruit peel has not been used and tends to become waste. Inside the rambutan skin contains saponins, flavonoids, and tannins. The purpose of the reserchto analyze the amount of alveolar macrophage in the mouse exposed to cigarette smoke.
Methods: The samples in this study were 25 male white rats of wistar strain divided into 5 groups including control group (K1), negative control group (K2), and 3 treatment groups (P1, P2, and P3) treated with rambutan skin extract with variation consecutive doses of 3, 6, and 12mg/200g BB and daily tobacco smoke exposure for 30 days.the amount of macrophage alveoler data was analyzed by One Way Anova analysis and continued with LSD advanced test.
Results: The result of LSD test showed that alveolar macrophage level in K1 group (41,76 ± 0,75) was significantly different with group K0 (31,72 ± 0,65), P1 (37,00 ± 0,54), P2 (35,52 ± 0.48), and P3 (30.32 ± 0.80). Rambutan peel extract contains antioxidants as protection against oxidative stress on alveoli macrophages due to exposure to cigarette smoke. At a dose of 3mg/200gram BB.
Conclusion: The rambutan peel extract effectively decreases the level of alveolar macrophage in the lung of the mouse exposed to cigarette smoke

Keywords: Antioxidant, rambutan, macrophage alveolar, smoke cigarette.

P036

Mitochondrial Function Differences between Autism and Non-autism Lymphoblastoid Cell Line

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Background: Autism spectrum disorder (ASD) is characterised by lasting problems with social communication and social interaction, restricted and repetitive behaviours, and symptoms become apparent only at the age of 2. Recently, mitochondrial dysfunction (mtD) has been proposed to explain the connection between the diverse medical symptoms associated with ASDs. Currently it is believed that mtD may be present in up to 80% of children with ASD and around 5 to 10 percent of children with autism have mtD as the underlying cause of their symptoms.
Methods: We compared the mitochondrial function and respiration of the lymphoblastoid cell line of children with autism (ALCL), and their developmentally normal non-autistic siblings (NALCL) using a modular instrument for high-resolution respirometry, Oxygraph-2k (O2k).
Results: Our results showed that the OXPHOS capacity (P) and ETS capacity (E) of ALCL is significantly higher compared to NALCL ($p<0.01$). In an experiment measuring the CII-linked respiration rate and mitochondrial membrane potential (MMP) simultaneously, the CII-linked P and E are higher in ALCL compared to NALCL ($p<0.01$) although MMP does not show significant difference between the two states of respiration. In addition, complex IV activity was found to be higher in ALCL as compared to NALCL ($p<01$).
Conclusion: In conclusion, the overall activity in the pathway generating ATP in ALCL is higher than in NALCL except for the MMP leading to the mtD.

Keywords: Autism, mitochondria, oxidative stress, OXPHOS, electron transport system.

P037

Effects of Insulin/insulin-like Growth Factor-1 Signaling Pathway Genes on Lifespan of *Caenorhabditis elegans*: A Systematic Review

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Background: Insulin/insulin-like growth factor-1 signaling pathway (IIS) or also known as IGF-1 signaling pathway plays a major role in aging. Genes in this pathway has been shown to affect longevity in previous researches. The purpose of this review is to determine the role of IIS pathway on the lifespan of *Caenorhabditis elegans*.

Methods: Literature search for relevant studies was done through PubMed and Scopus databases using mesh keywords *Caenorhabditis elegans*, *C. elegans*, nematode, genes, RNA, DNA, IIS pathway, IGF pathway, lifespan, longevity. After exclusion of duplicates, review papers, human studies, *in vitro* studies and studies using other organisms, a total of 71 research articles were assessed. Data relevant to effects of insulin/insulin-like growth factor-1 signaling pathway genes on lifespan of *Caenorhabditis elegans* was independently extracted.

Results: Results of the review indicated that *daf-2*, *hsf-1* and *skn-1* significantly influenced the lifespan of *Caenorhabditis elegans*. These longevity-associated genes were found to be conserved across species. A total of 10 studies found that *skn-1* and *hsf-1* knocked down mutants have a shortened lifespan. A total of 19 studies showed that reduction in daf-2 gene activities extended the lifespan of *C. elegans*.

Conclusion: Genes in IIS pathway influence the lifespan of *C.elegans* where upregulation of *hsf-1* and *skn-1* as well as knockdown of *daf-2* resulted an increased lifespan while knockdown of hsf-1 and skn-1 resulted a shortened lifespan.

Keywords: *Caenorhabditis elegans*, *C. elegans*, nematode, genes, RNA, DNA, IIS pathway, IGF pathway, lifespan, longevity.

P038

Chemopreventive and Hypolipidaemic Effects of *Piper Betle* in Obesity-AOM (Azoxymethane) induced Colon Cancer Rats

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Background: *Piper Betle* contains many bioactive compounds with anticancer and antioxidant properties. The aim of this study was to determine whether *Piper Betle* supplementation to obesity-induced colon cancer rats can reduce aberrant crypt foci (ACF) and its associated lipid and tumor markers.
Methods: Seventy two 3-week-old male Sprague Dawley rats were divided into eight groups: 1) Normal diet, 3.8 kcal/g; 2) *Piper Betle* fed diet (PBD) (150 mg/kg BW); 3) Azoxymethane (AOM)-induced colon cancer; 4) AOM and PBD; 5) High Fat Diet (HFD), 5.2 kcal/g; 6) HFD and PBD; 7) HFD and AOM; and 8) HFD + AOM + PB. AOM (15 mg/kg) was injected into rats via intraperitoneal (i.p) once a week for 2 weeks after three months of supplementation. Confirmation of ACF in colon cancer tissues was performed using Methylene blue staining. Rats were fed with *Piper Betle* via oral gavage for three months. All rats were sacrificed after supplementation and blood and tissues were collected for the determination of ACF and lipid profile.
Results: Total serum cholesterol, LDL (low density lipoprotein) and TG (triglycerides) levels increased significantly ($p<0.05$) in HFD group when compared to the normal diet group. Interestingly, supplementation with PB decreased total cholesterol and LDL levels significantly in HFD group. HFD diet reduced HDL significantly in serum of rats when compared to normal diet but PB increased its level significantly ($p<0.05$) in all groups when compared to HFD group. ELISA determination of leptin showed that it increased significantly ($p<0.05$) in HFD and AOM groups but decreased significantly ($p<0.05$) when treated with PB. Treatment with PB also reduced the number of ACF seen in colon cancer rats.
Conclusion: Our findings demonstrated that *Piper Betle* has anticancer and hypolipidaemic effect in obesity-AOM induced colon cancer rats.

Keywords: Obesity, colon cancer, *Piper betle*, ACF, leptin.

P039

Peripheral Blood Gene Microarray Reveals Inflammation and Signal Transduction Pathway is Associated with Cognitive Decline in Normal Ageing

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Background: Declined cognitive function during ageing is multi-factorial and gene expression changes are one of the factors influencing this trajectory event in the absence of neurodegenerative disease. Identifying these genes and biological processes involved in this study would explain certain individuals resilient to the age-related cognitive decline.

Methods: A cross sectional study was carried out on 160 Malay healthy subjects aged between 28 – 68 years old who were recruited after screening 1768 volunteers around Selangor and Klang Valley. Out of that, 72 subjects were included for microarray study who were divided into four groups according to their age. They were further divided into normal cognitive (NC) (score>24) and impaired cognitive (IC) (score <24) groups based on Montreal Cognitive Assessment (MoCA). Blood samples for total RNA extraction were collected and gene expression analysis was performed by using Illumina HT-12 Bead Chips. Partek Genomic software was used to perform gene expression profiling analysis and the overrepresentation of genes expression was analysed further to identify altered pathway by using Pathway Studio.

Results: Transcriptomic data revealed that gene expression pattern in subjects with cognitive impairment have a unique molecular state from normal cognitive aging at early age of 30. Most of the top differentially expressed genes in group G30IC vs G30N were upregulated while most of the top genes in group G60IC vs G60N

were downregulated. Subjects with cognitive impairment exhibited prominent upregulation in the expression of genes associated with inflammation, ion channel activity, ion utilization and oxidative stress while decreased expression of several genes involved in DNA repair, signal transduction and synaptic transmission.
Conclusion: In conclusion, our data revealed that there is an incidence of about 21.88% of the Malay population with cognitive decline as corresponding molecular alteration that classifies normal cognitive and cognitive impairment subjects.

Keywords: Peripheral blood, microarray, inflammation, signalling pathway, cognitive decline

P040

Different Viability Response on Antioxidant and Oxidant exposure in Autism Lymphoblastoid Cell Lines with the Non-Autistic Sibling

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Background: Autism Spectrum Disorder is a neurodevelopmental condition which is associated with oxidative imbalance between oxidant and antioxidant. It has been proven that Tocotrienol-rich Fraction (TRF) as antioxidant properties by *in vitro* and *in vivo* study.
Methods: In this study, a single pair of Lymphoblastoid Cell Lines (LCLs) from children with autism (ALCLs) and their non-autistic (NALCLs) sibling purchased from Autism Genetic Resource Exchange (AGRE) were used and cultured in RPMI-1640 tissue culture medium. Cells were divided into 4 groups: Cell treated with: TRF, Hydrogen Peroxide (H_2O_2), Pre-treatment (TRF and H_2O_2), and Post-treatment (H_2O_2 - TRF). Cell were incubated with antioxidant containing medium; 0, 1, 2, 4, 6, 8, 10, 20 µg/ml of Tocotrienol Rich Fraction (TRF) for 24 h and oxidant containing medium; 0, 50, 100, 150, 200, 250, 300, 350 µM (H_2O_2) for 1 h.
Results: The viability test on ALCLs showed that the proliferation of ALCLs was increased at 8 µg/ml TRF ($P = 0.009$) compared to untreated control. The viability cells also increased at 6 µg/ml ($P = 0.0171$), 10 µg/ml ($P = 0.0328$), and 20 µg/ml ($P = 0.0299$). However, there was no significant effect on the viability of the NALCLs after treated with TRF. On the other hand, the hydrogen peroxide reduced the proliferation of the ALCLs and the NALCLs with the same IC50 at 150 µM (47%, $P = 0.009$). The viability cells started decreased at 50 µM (83%, $P = 0.001$), and 100 µM (62%, $P = 0.00313$).
Discussion: These findings suggested that TRF exhibited selective effect on ALCLs with positive response in increasing the viability of cells while no effect was seen on the normal cells. TRF might restore the antioxidant activity in ALCLs thus increasing the proliferation capacity of the cells. Unlike NACLCs, the exogenous antioxidant might not alter the proliferation capacity which was already in the optimum level. Amount of H_2O_2 exposure to both of the cells imposed the same oxidative stress response that caused the decreased in proliferation that might be due to apoptosis, necrosis or growth arrest.

Conclusion: These results indicated that exogenous antioxidant supplementation might be beneficial on autism lymphoblastoid cells in restoring the optimum proliferation capacity.

Keywords: Autism, Autism Lymphoblastoid Cell Lines, Tocotrienol Rich Fraction

P0041

40 Days of Raisins Consumption on Human Plasma MDA Level

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Background: Human body is continuously exposed to many free radicals which resulted in oxidative stress that lead to certain diseases. Antioxidants are very importance to overcome this condition. In this study, we aim to investigate the effect of consuming 7 seeds of raisins per day over 40 days, as a source of natural antioxidant on oxidative stress biomarker, plasma MDA.
Methods: This study is a quasi-experimental study design (Pretest-Posttest). 31 subjects were enrolled in this study. After consent, data including demographic data, health status, diet intake, lifestyle and other environment factor were collected using a set of questionnaire. Then, the blood was collected and physical health measurements (BMI, blood pressure, heart rate) were measured. After that, the subjects were required to consume 7 seeds of raisins daily in the morning for a period of 40 days. As part of raisin consumption method, subjects were required to recite 'basmalah' followed by three times of *shalawat* before consuming the raisins. Blood collection and physical health measurements were done again after the 40 days period. The blood was used to measure MDA level using TBARS assay. In addition, antioxidant activity of raisins that consumed by the subjects was also tested using DPPH assay using calamansi lime as control.
Results: The results showed that the raisin extract had a relatively higher antioxidant activity (71.17 $\pm$ 2.790 µmol/L TEAC) compared to the Calamansi lime extract (10.61 $\pm$ 2.959 µmol/L TEAC). Furthermore, prior raisin consumption, the mean OD for MDA level of subject was 0.910 $\pm$ 0.398 and this level was significantly lower (0.592 $\pm$ 0.259) after 40 days of raisin consumption (p=0.000). The result for physical health measurements showed no significant differences for all the physical health measurement between pre and post 40 days of raisins consumption.
Conclusion: Antioxidant content of raisins could reduce plasma MDA level after 40 day of consumption.

Keywords: Raisin, oxidative stress, plasma malondialdehdye, TBARS assay, antioxidant

P0042

The Potency of Green Tea Leaf Extract (Camilia sinensis, L) to Morphology and MDA Levels in Rat (Rattus novergicus) Lungs after Cigarette Smoke Exposure

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Background: Free radicals from cigarette smoke can cause lipid peroxidation of bilayer membranes that is characterized by elevated levels of malondialdehyde (MDA). Green tea leaves contain catechin flavonoids, it's an antioxidant that can reduce free radicals. The purpose of this research is to know the potency of green tea extract (Camilia sinensis) to morphology and MDA level in rat lungs after exposed by cigarette smoke.
Methods: This reseach is experimental study, using 30 rats that were divided into control (K) and 4 treatment group (cigarette smoke /P1; green tea extract at dose 200 mg/kg bw, P2; cigarette smoke and green tea extract at dose 200 mg/kg bw, P3; cigarette smoke and green tea extract at dose 400 mg/kg bw, P4). The exposure of cigarette smoke is acted by burning 3 cigarettes per group for 30 and 45 days. The morphology of lungs is observed by calculating the extent of patches of blackish spots. MDA levels were measured by TBA (Thiobarbituric Acid) test and data analysis by t-student test.
Results: The results showed that green tea leaf extract was not able to reduce the extent of blackish spots on the surface of the rat lungs ($p = 0.351$, $p > 0.05$). Green tea leaf extract decreased significantly MDA level in rat lungs ($p = 0.03$, $p < 0.05$) at dose of 400 mg/kg bw (6,3725 nmol/mL to 4,485 nmol/mL) after cigarette smoke exposure.
Conclusion: Green tea leaf extract decrease potentially MDA level in rat lungs after cigarette smoke exposure.

Keywords: Green tea, lung, MDA, cigarette smoke.

P0043

Differential Protein Expression Profile in Mature Neuronal Cell Model of Alzheimer's Disease and Its Modulation by Alpha-Tocotrienol

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Background: The development of differentiated cell model of Alzheimer's disease (AD) into mature neuron using stable transfected SH-SY5Y is crucial to provide an appropriate *in vitro* model that mimics the pathology of neurons in AD. This study aimed to determine the effect of selected vitamin E isomer; alpha-tocotrienol on the proteomic profile of differentiated mature neuronal model of AD developed from SH-SY5Y cell.
Method: Untransfected SH-SY5Y, stably transfected SH-SY5Y with plasmid APP *wildtype* and APP *swedish/indiana* were differentiated and further screened with α-, γ- and δ- tocotrienol. α-Tocotrienol treated and untreated mature neuronal cells were subsequently analysed for proteomic profile using liquid chromatography mass spectrometry (LCMS/MS).
Results: Proteomic analysis between untreated untransfected cells and untreated *wildtype* showed significant changes in apoptotic pathway involving proteins such as apoptosis inducing factor (AIFM1), caspase 3 (CASP3), Bcl-2 related X (BAX), DIABLO, insulin growth factor receptor (IGFR2) and subunit from HSP70 which are HSPA1A, HSPA8 and HSPA5. Meanwhile comparison between untreated untransfected cells and untreated *swedish/indiana* showed that proteins involved in the negative regulation of catabolic process of APP were differentially expressed. Comparison between untreated *wildtype* and untreated *swedish/indiana* revealed the differentially expressed proteins were mainly involved in oxidative stress, apoptosis and metabolic processes. Comparison beween untransfected α-tocotrienol treated and untreated mature neuronal cell showed that proteins involved in apoptosis pathway through Fas signalling pathway; CASP3, gelsoline (GSN), lamine nuclear (LMNA, LMNB1) and poly-ADP-ribose polymerase 1 (PARP1) were differently expressed while comparison between untreated and α-tocotrienol-treated *wildtype* showed proteins involved in the regulation such as ubiquitin proteasome, cell cycle and Parkinson's disease pathway and other pathways such as cell structure (axonal guidance by semaphorins and cytoskeletal regulation by Rho-GTPase) and metabolic (Kreb's cycle and glycolysis) were differently expressed. For comparison

of untreated and α-tocotrienol-treated *swedish/indiana*, the differentially expressed proteins were involved in biological processes such as anatomical structure development, maintenance of telomere length and apoptosis signalling pathway and in other pathways such as axonal guidance mediated by semophorin (collapsing response mediator protein (CRMP1), dihydropyrimidinase like 3 (DPYSL3), and cyclin dependent kinase 5 (CDK5)) and regulation of cytoskeletal by Rho GTPase (actin (ARPC1A and ACTBL2), tubuline (TUBB), CDC42 and cofillin (CFL2)).
Conclusion: α-Tocotrienol plays a role in regulating protein expression in Alzheimer's disease mature neuronal cell model especially involving neuronal structural changes indicating its role in delaying the progression of the disease.

Keywords: SH-SY5Y, APP, Mature Neuron, Alpha-Tocotrienol, LCMS

V001

Measurement of Oxygen Consumption Rate in Mitochondria of Rat Hippocampus using High-resolution Respirometer

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Background: Mitochondrial dysfunction in hippocampus has been associated with aging. Oxygen consumption rate (OCR) is one of the widely used parameter to indicate the mitochondrial function. Traditionally OCR is measured using a cumbersome Clark electrode. High resolution respirometry (HRR) offers greater sensitivity and flexibility for substrate-uncoupler-inhibitor titration (SUIT) protocol. However, the method of measuring mitochondria isolated from rat hippocampus using HRR is not available. In this study we aimed to demonstrate the measurement of OCR in mitochondria isolated from rat hippocampus using HRR Oxygraph-2k (O2k).
Methods: Hippocampus of 12 weeks old Sprague-Dawley Rats was dissected out and the mitochondria were isolated by sucrose step density gradient centrifugation method. OCR of the isolated mitochondria was measured by OROBOROS O2k usinhg SUIT protocol. The eef t of two different respirometry media, MiR05 and MiR05Cr (with creatine), was compared.
Results: OCR of the isolated mitochondria was higher in Complex I-linked respiration following the addition of glutamate, pyruvate and malate, in ADP-stimulated coupled respiration, in Complex II-linked respiration by succinate, and maximal respiration wsas achieved by titration of CCCP uncoupler. OCR was lower during proton leak state induced by oligomycin, while residual respiration was achieved by the addition of rotenone and antimycin A to inhibit complex I and III, respectively OCR was not different between MiR05 and MiR05Cr.
Conclusion: Our results demonstrate that HRR O2k can be used successfully on mitochondria isolated from rat hippocampus to measure OCR.

Keywords: Oxygen consumption rate, high-resolution respirometry, hippocampus, mitochondria.

V002

Inhibition of Cytoglobin Gene Expression in Human Keloid Fibroblasts Using siRNA and its Effect on Cell Proliferation : a Preliminary Study

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Background: In our previous work, we found the expression of Cytoglobin (Cygb) in keloid were significantly higher than those in normal skin, which accompanied by high rate of fibroblasts cells proliferation. Therefore, we plan to elucidate the role of Cygb in the regulation of keloid fibroblast proliferation using small interfering RNA (siRNA). The aim of this study is to ensure the dose of siRNA that we should be used in the next work.
Methods: Inhibition of cytoglobin expression was achieved by using siRNA targeting Cygb (siCygb Santacruz®). We compared the relative expression of Cygb between three various doses of siRNA (10 pmol, 20 pmol, and 40 pmol) and control group. Expression of cytoglobin was measured by real-time polymerase chain reaction with Livak formula and cells proliferation was counted by dye exclusion method. All assay were performed according to the manufacturer's protocol and were done in duplicate.
Results: The expression level of Cygb after administration of siRNA were decreased in all doses group (10 pmol, 20 pmol and 40 pmol) compared to control group (0.04 $\pm$ 0.01, 0.17 $\pm$ 0.01, 0.66 $\pm$ 0.07, and 1 respectively), with an unexpected decrease pattern. We suspect there is some sort of protection mechanism that is triggered when large amounts of siRNA were introduced into cells, that should confirm in further study. Whereas the cells proliferation were decreased slightly in all doses group after normalization to control group (0.98 $\pm$ 0.09, 0.76 $\pm$ 0.17, 0,76 $\pm$ 0.02 and 1 respectively).
Conclusion: All doses of siRNA that is used in this study were successful to suppressed cytoglobin gene expression in human keloid fibroblast cells with varying effect levels. We decide to use the second dose (20 pmol) for the subsequent study.

Keywords: Human keloid fibroblasts, siRNA, cytoglobin, proliferation.

V003

Bovine Liver Cytoglobin is Recognized by anti Mouse anti Human Cytoglobin Antibody

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Background: Cytoglobin (Cygb) is a relatively recent discovered extra erythrocyte hemoglobin in vertebrata, which is expressed in various types of tissue and whose function is still unclear. However, Cygb may function in detoxification of nitrite oxide (NO), reactive oxygen species (ROS) and as intracellular oxygen storage, which is usually very important in hypoxia. To study these functions, the pure form of Cygb is needed. For this purpose, we isolated and purified of Cygb from bovine liver.
Methods: Cygb was isolated and precipitated from bovine liver by addition of ammonium sulphate (50%, 70%, and 90%). Then, Cygb was purified using anion exchange chromatography (DEAE Cellulose), followed by immunoaffinity chromatography using anti mouse anti human Cygb antibody.
Results: In this study, we showed that anti mouse anti human Cygb antibody can recognize and bind specifically the bovine liver Cygb.
Conclusion: We conclude that anti mouse anti human Cygb antibody could be used to purify bovine liver Cygb.

Keywords: Cytoglobin, purification, DEAE Cellulose, Immunoaffinity.

V004

Expression of Cytoglobin in PHA Induced Mytotic Human Lymphocytes

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Background: In specific immune respons, lymphocytes undergo many activities such as mytosis, synthesis and secretion of a number of proteins. All of this activities requires a large amount of energy which can only be supplied by aerobic metabolism. Since the oxygen supply from the environment is constant, and oxygen demand increases, the lymphocytes are in relative hypoxia. For this purpose, cells must have a compound which, like hemoglobin, bind oxygen more tightly. Such proteins, called as extra erythrocyte hemoglobin, and one of them is cytoglobin.
Methods: PBMC is isolated from peripheral blood by sentrifugation with ficoll and PHA (phytohaemagglutinin) is used to induce mytosis. PBMC is incubated with PHA for 24, 48, and 72 hours to ensure cell proliferation. Cytoglobin is measured by ELISA and is compared with control group.
Results: The result shows that there is an increment of cytoglobin in mytotic lymphocytes. There is an increase of cytoglobin in 24 hours, in PHA induced lymphocytes compared to control group. In 48 hours, the increment is higher than 24 hours. In 72 hours the increment is lower than 48 hours, but still higher than 24 hours.
Conclusion: It is suggested that cytoglobin does increase in mytotic cells to overcome hypoksia, and in this research it is observed that its peak is at 48 hours.

Keywords: Cytoglobin, hypoxia, mytosis, lymphocytes

V005

Analysis and Correlation between TGF-β, TGF-β Receptor 2 Concentration, and Relative Expression of SMAD2 mRNA on Pre-eclamptic Placenta

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Background: The presence of abnormalities in the placental growth process is one of the theories causing preeclampsia. Presumably there are antiangiogenic factors that play a role in the failure of this pseudovasculogenesis. Previous research has shown an increase in TGF-β but can't confirm the success of signal transduction. The purpose of this study was to examine the possibility of signal transduction interference TGF-β via SMAD2.
Methods: A total of 34 normal placental samples and 34 placental preeclamptic samples were examined for TGF-β and TGF-β receptor 2 using ELISA. In addition, to see the relative expression of SMAD2 mRNA the RT-PCR method is used. We compared the results of normal placental examination with preeclampsia and then correlated the parameters.
Results: Significant differences in levels of TGF-β (N=2,427 pg/mg; PE=4,391 pg/mg; p=0,0001) and TGF-β protein receptor 2 (N=1,269 pg/mg; PE=1,874 pg/mg; p=0,0001) in placenta preeclampsia versus normal placenta. Both TGF-β and TGF-β Receptor 2 have an increase in placenta preeclampsia. The same thing was also obtained from examination of the relative expression of SMAD2 mRNA that increased in placenta preeclampsia (Livak: N=1; PE=1,49; p=0,033). From the correlation test found a mild positive correlation between TGF-β protein level with the relative expression of SMAD2 mRNA in normal placenta (p=0,022 R=0,347).
Conclusion: TGF-β protein level, TGF-β Receptor 2 and relative expression of SMAD2 mRNA have increased in placenta preeclampsia. It found a mild positive correlation between TGF-β protein levels and the relative expression of SMAD2 mRNA in normal placenta, but not found in preeclamptic placenta. There may be other factors contributing to SMAD2 mRNA expression regulation.

Keywords: TGF-β, TGF-β Reseptor 2, SMAD2 mRNA, preeclampsia.

V006

The Use of an Antioxidant Polyherbal Remedy, *Aphayathikun*, in Patients with Mild to Moderate Lower Urinary Tract Symptoms (LUTS): Case Series

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Background: Age-related oxidative stress has been noted as an important cause of lower urinary tract symptoms. A polyherbal decoction named '*Aphayathikun* (AP)' has been recorded in Thai traditional medical system for treatment of urinary ailments. This study was aimed to preliminary investigate *in vitro* antioxidant capacity of AP and report an observation from a case-series of five patients with mild to moderate lower urinary tract symptoms (LUTS).
Methods: *In vitro* antioxidant activity of AP decoction were done by DPPH, ABTS, metal chelating, and FRAP assays. The International Prostate Symptom Score (IPSS) was used as an observational tool. Patients with mild to moderate LUTS who had a history of continuously consumed 90 mL per day of the AP for at least 7 days were included in this study. IPSS and quality of life (QoL) scores of each patient were discussed within 1 month after the consumption period. The historical record of serum biochemistry, haematological parameters, and urine analysis were additionally discussed.
Results: *In vitro* antioxidant analyses carried out revealed that AP decoction and its herbal components exhibit notable antioxidant activities. The continuously consumption of AP decoction for 7 days may affect the patient's actual symptoms score. Our results revealed that both the IPSS of QoL scores of these patients had decreased (8.6 ± 3.9 *vs.* 1.4 ± 2.2, $p = 0.003$ for IPSS and 3.8 ± 1.3 *vs.* 1.8 ± 0.8, $p = 0.003$). There were no changes observed on serum biochemistry, haematological, and urine analysis parameters.
Conclusion: Findings of case series studies reported in this work can be used to generate hypotheses for further research on determination of the effectiveness and safety of the antioxidant polyherbal mixture, *Aphayathikun*.

Keywords: Antioxidant activities, traditional polyherbal formula, LUTS, Aphayathikun, Traditional Thai medicine.

V007

Assessment of Antioxidant Activities and Beneficial Health Effects from the Consumption of Local Polyherbal Infusion 'Suk-Jai'

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Background: It is well-established that oxidative stress in obesity is an important cause of obesity-related non-communicable diseases, in particular cardiovascular diseases. Suk-Jai (SJ) is polyherbal infusion made from four edible plants including *Carthamus tinctorius* (flowers), *Pandanus amaryllifolius* (leaves), *Caesalpinia sappan* (wood), and *Aegle marmelos* (fruit). The infusion normally consume by local people in Ranot District, Songkhla. The objective of this study was to evaluate *in vitro* antioxidant capacity of SJ and report an observation of its beneficial health effects in hyperlipidemia consumers.
Methods: Antioxidant capacity of SJ infusion were evaluated by DPPH, ABTS, metal chelating, and FRAP assays. The preliminary screening of phenolics and flavonoids contents were additionally measured. The lipid profiles, BMI, and fasting blood glucose levels of consumers that had a history of continuously consumed at least on a cup (125 mL) this infusion per day for at least 8 weeks were discussed in this study.
Results: SJ infusion exhibited potent antioxidant activity with IC_{50} of 1.6 $\pm$ 0.05 mg/mL for DPPH assay and 0.53 $\pm$ 0.01 mg/mL for ABTS assay. The metal chelating activity and ferric reducing power of the infusion were 0.51 $\pm$ 0.01 mg/mL (IC_{50}) and 336.69 $\pm$ 2.79 mg $FeSO_4$/g extract, respectively. There were no notable effects observed on BMI of the volunteers, while the reduction of total cholesterol were observed in seven out of nine volunteers.
Conclusion: Promising antioxidant capacity of the local infusion was found in this present work, however, there were no notable beneficial effects toward the consumers observed in this study.

Keywords: Antioxidant activities, polyherbal infusion, herbal tea.

V008

Gynura procumbens Standardized Extract Reduces Lipid Peroxidation and Cholesterol Level in Atherosclerotic Rat Model

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Background: Lipid peroxidation resulted from reactive oxygen species (ROS) action on membrane cell due to overproduction of ROS. It plays a role in the development of atherosclerosis whereby the oxidation of LDL-cholesterol by ROS promotes atherosclerotic plaque formation. *Gynura procumbens* (GP) has been reported to have anti-hyperlipidaemic, hypertensive, cardio-protective effect, antioxidative, anti-hyperglycemic and anti-inflammatory properties. GP might have an ability to reduce lipid oxidation and prevent atherosclerosis. This study is to determine the effect of GP standardized extract lipid peroxidation and cholesterol level in the atherosclerotic rat model.
Methods: Forty-eight female Sprague Dawley rats were divided into sham with (1) basal diet, (2) 250GP; (3) 500GP; (4) atorvastatin (ATV); and atherosclerotic rat model with (5) 2%CHO5HPO; (6) 2%CHO5HPO250GP; (7) 2%CHO5HPO500GP; (8) 2%CHO5HPOATV. Treatment was given for 24 weeks. Blood pressure was taken monthly and blood was collected through orbital sinus at 0, 3 and 6 months. The plasma MDA level was measured by HPLC. Cholesterol level (total cholesterol, LDL-cholesterol and HDL-cholesterol) and total triacylglycerol (TG) was measured using spectrophotometer.
Results: Blood pressure was increased starting from the first month in atherosclerotic rat model (2%CHO5HPO) and reduced with extract supplementation. Serum total cholesterol, TG, LDL-cholesterol and MDA level were increased at 3 and 6-month duration in atherosclerotic rat model and was reduced with extract supplementation. GP extract increased serum HDL-cholesterol level in atherosclerotic rat model compared to the atherosclerosis group.
Conclusion: GP extract supplementation with the dose of 500 mg/kg body weight gave better effect than the lower dose (250 mg/kg body weight). Standardized extract of *Gynura procumbens* is able to reduce lipid peroxidation and cholesterol level in atherosclerosis.

Keywords: Atherosclerosis, *Gynura procumbens*, Oxidative stress, Cholesterol.

V009

Administration of Jackfruit (*Arthocarpus Heterophilus*) Tree Bark Extract Cream Prevents the Increase of Melanin Amount in Guinea Pig (*Cavia Porcelus)* Exposed by UV-B Ray

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Background: Jackfruit (*ArtocarpusHeterophillus)* tree bark ethanol extract contains antioxidant, phenolic, *tannin,* steroid, linoleic acid ethyl ester *and also vitamin C,* it can inhibit the increase of melanin amount in melanocyte while hydroquinone is used as the gold standard for hyperpigmentation treatment until now. This research aimed to study whether the administration of jackfruit tree bark extract cream can inhibit the increase of melanin amount in guinea pig exposed by UV-B ray and compared the effectivity of jackfruit tree bark extract cream 4% with hydroquinone cream 4%.

Methods: This study was an experimental laboratory research by using randomized post test only group design. The independent variable is the jackfruit tree bark extract cream dose and the hydroquinone cream, while the dependent variable is the melanin amount in epidermal layer. A total of thirty guinea pigs (*Cavia Porcelus*) used in this study were split into 3 groups consisted of 10 male guinea pigs in each group, which were one treatment control group administered with basic materials cream and two treatment administered with hydroquinone cream 4% and jackfruit tree bark extract cream 4%. All of the treatment group were exposed by UV-B ray with total dose of 390 mJ/cm^2 for 2 weeks, and then biopsy was undergone to examine melanin amount in epidermal layer. One way ANOVA was used to analyze difference between control group and treatment group 1 and 2 and continued with Least significant Difference (LSD) was used to analyze the existence of treatment difference after treatment ($p<0,05$).

Results: Result of the study showed that melanin amount of the group control was 54.33 $\pm$ 4.52% Significant decrease in the mean of melanin amount in treatment group 1 was 3.01 0.89% In treatment group 2 there was 4.23 $\pm$ 1.82% of melanin amount. The difference between control group and treatment group 1 and 2 was

significant in decreasing the melanin amount in epidermal layer ($p<0,05$). In the treatment group 1 and 2 wasnot significant in decreasing the melanin amount in epidermal layer ($p>0,05$).

Conclusion: The conclusion of this study was that 4% jackfruit tree bark ethanol extract cream could decreased melanin amount in epidermal layer. Administration of 4% jack fruit tree bark ethanol extract cream had the same effectiveness with 4% hydroquinone cream prevented the increase of skin melanin in guinea pig.

Keywords: Jackfruit tree bark extract cream, melanin amount, UV-B ray.

V010

Administration of Breadfruit Leaves Extract (*Artocarpus Altilis*) Cream Prevented the Increase of Skin Melanin in Guinea Pig (*Cavia Procellus*) Exposed to Ultraviolet B (UVB)

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Background: Skin is the main target of environmental influences, especially by ultraviolet (UV) ray that result the abnormality of hiperpigmentation such as lentigo and melasma. In pathology, hyperpigmentation is caused by an increasing in the amount of melanin. Hydroquinone is the gold standard for hyperpigmentation disorders, but using it for a long period will make adverse effects such as ochronosis. Based on phytochemical and chromatography research, breadfruit leaves extract contains active ingredients that can work in synergy prevented the increase of melanin. Because of that, breadfruit leaves extract was a strong candidate as an antioxidant and whitening agent. The purpose of this research was to prove the effect of administration of breadfruit leaves extract (*Artocarpus altilis*) cream prevented the increase of skin melanin in guinea pig (*Cavia procellus*) exposed to ultraviolet B and to prove the administration of breadfruit leaves extract (*Artocarpus altilis*) cream have the same effectiveness with 4% hydroquinone cream in preventing the increase of skin melanin in guinea pig (*Cavia procellus*) exposed to ultraviolet B.
Methods: This study was a true experimental research using post test only control group design. The subjects were devided into three groups, with 10 guinea pigs each group. Group 1 as a control group was treated by UVB exposure and basic cream. Group 2 was treated by UVB and 4% hydroquinone cream. Group 3 was treated by UVB and 3% breadfruit leaves extract cream. Total 390 mJ/cm^2 ultraviolet B dosage was given for 2 weeks. The amount of melanin was examined by histopatological method with Masson-Fontana staining, counting the melanin area by black color. The amount of melanin was calculated by the percentage of the pixels area of melanin and was compared with the pixels of all the epidermal tissues.
Results: The results showed that the highest number of melanin was in the group 1 (44,45 $\pm$ 3,81). The amount of melanin in group 3 was 3,02 $\pm$ 1,75. The lowest

number of melanin was in group 2 (0,78 ± 0,60). There was significant difference within control group compared with group 2 and 3 (p<0,05). There was no significant difference within group 2 compared with group 3 (p>0,05).
Conclusion: In conclusion, the administration of 3% breadfruit leaves extract (*Artocarpus altilis*) cream prevented the increase of skin melanin in guinea pig (*Cavia procellus*) exposed to ultraviolet B. The administration of 3% breadfruit leaves extract (*Artocarpus altilis*) cream had the same effectiveness with 4% hydroquinone cream. The result of this study could be applied as a clinical trial, a basis for further study in pursuit of mechanism and other effect of breadfruit leaves extract cream.

Keywords: Breadfruit leaves extract cream, melanin, ultraviolet B, guinea pigs.

V011

Exploring the Potential of Vitamin E Isomers α-Tocopherol and γ-Tocotrienol in Preventing Peri-Implant Osteolysis *in vitro*

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Background: Aseptic loosening is a major complication in those who underwent arthroplasty with polyethylene-based prosthesis following excessive bone resorption by osteoclasts. Vitamin E are known to possess antioxidant and anti-inflammatory properties. This study was aimed to determine whether vitamin E isomers α-tocopherol and γ-tocotrienol exhibit inhibitory effects on osteolasts that are exposed to polyethylene.
Methods: Peripheral blood mononuclear cells were extracted from blood of a healthy. The cells were cultured in presence of 25 ng/ml MCSF and 50 ng/mL RANKL on collagen gel-precoated plate with and without polyethylene. Some cells exposed to polyethylene were treated with either 50 M α-tocopherol or γ-tocopherol beginning from the 7th day of cell culture. Number of osteoclasts formed on day 14 was assessed from staining of osteoclast marker TRAP. Osteoclast activity was assessed from percentage of total area of resorption pits on bone pieces viewed through scanning electron microscope.
Results: Examination from the TRAP staining found that the formation of multinucleated TRAP-positive osteoclast-like cells. Treatment with either tocopherol or γ-tocopherol did not change the number of osteoclasts formed. Nonetheless examination on resorption pits found that there was complete inhibition of resorption pits formation in α-tocopherol and γ-tocotrienol treated groups.
Conclusion: Data from this study indicated that treatment with either α-tocopherol or γ-tocotrienol suppresses the activity, but not formation, of osteoclasts exposed to polyethylene. This finding may suggest the potential of α-tocopherol and γ-tocotrienol in preventing polyethylene-induced peri-implant osteolysis which can be benefited by millions of patients undergoing joint replacement.

Keywords: Osteoclasts, polyethylene, osteolysis, tocopherol, tocotrienol.

V012

Oxidative Stress & Antioxidant in Autism Spectrum Disorder (ASD)

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Background: Autism spectrum disorder (ASD) is lifelong wide spectrum neurodevelopmental disorder characterized by (i) persistent deficits in social communication and social interaction, and (ii) restricted, repetitive patterns of behaviour, interests or activities. Various studies suggested ASD to be multifactorial which include the interaction among genetic, familial autoimmunity, metabolic derangement, inflammation, impaired detoxification, environmental factors and oxidative stress. Oxidative stress occurs when reactive oxygen species (ROS) level exceeds the antioxidant capacity of a cell. The increased production of ROS both centrally (in the brain) and peripherally) may result in the reduction of brain cell number, leading to autism pathology. Thus, systematic review is conducted to identify the levels of oxidative stress biomarkers and antioxidants with the effects to the children with ASD compared to typically-developing children.
Methods: Google Scholar (2008 to 2018). The keywords oxidative stress, antioxidant, ASD and brain were used. Inclusion and exclusion criteria are indicated to narrow down the search. Four reviewers screened the title and abstract of all records identified by the search strategy. Full text copies of potentially relevant articles were obtained and screened. Outcome of the studies were summarised and tabulated.
Results: Malonyldialdehyde was found to be elevated, and levels of transferrin and ceruloplasmin were significantly reduced in children with autism, indicating that oxidative stress is increased in this disease. There was an increase in oxidative damage marker in the brain as evidence by increase in brain lipids (lipofuscin). Reduced level in enzymes that important in redox metabolism (glutathione peroxidase, glutathione S transferase, glutamate cysteine ligase) was also seen.
Conclusion: A number of studies have reported that biomarkers of oxidative stress correlated with autism severity. Several studies also showed that antioxidant therapies helped to improve the symptoms and behaviours of ASD.

Keywords: Oxidative stress, antioxidant, ASD.

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Oral

ACCURACY OF VIRTUAL BONE MEASUREMENT FROM CT SCAN IMAGES

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Introduction: In the application of scientific human skeletal variation in medico-legal matters, virtual anthropology is the current technique performed to examine skeleton and its body parts. Virtual anthropology can provide information normally unattainable using conventional method.
Objective: This study was conducted to compare measurements of bones by conventional method versus virtual method.
Methods: A total of 15 femora from the National Institute of Forensic Medicine, Hospital Kuala Lumpur were examined. Four parameters were measured i.e. maximum length of femur (*FeMl*), diameter of femoral head (*FeHd*), transverse diameter of midshaft (*FeMd*) and condylar breadth (*FeCb*). Osteometric board and vernier calipers were employed for conventional method, while CT scan and digital ruler in *Osirix MD* was yielded for virtual method. The measurements were repeated twice to calculate for inter and intra-analysis. For inter-observational analysis, two independent observers were employed to perform the measurements using each method in separate occasions.
Results: Results exhibited that there was no difference in measurements between the conventional and virtual methods. There was also no difference in the intra- or inter-observer error analyses. Technical error of measurement displayed values within the acceptable ranges (*rTEM* <1.5 for intra-observer and <2.0 for inter-observer), and the coefficient of reliability (*R*) had indicated small error in measurements (>0.95).
Conclusion: This brought to suggest that bone measurements by virtual method are as accurate and reliable as in the conventional method. This indicated that the virtual method may be utilised in forensic anthropology and for research studies.

Oral

WHERE IS THAT SNORE COMING FROM?

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Introduction: Frequency analysis of snores is a promising diagnostic tool for localizing the site of obstruction among snorers.
Objective: We aimed to map the origin of vibration in relation to frequency of snore among patients in Pusat Perubatan Universiti Kebangsaan Malaysia (PPUKM).
Methods: The snores (383 snores) of 40 participants were digitally recorded during natural and induced sleep, using a portable monitor (NOX-T3) with a built-in microphone. Upon recruitment, all participants underwent natural sleep study whereby the apnea-hypopnea index (AHI) and the mean frequency of 10 random snores on supine position were documented. Following that, drug induced sleep endoscopy (DISE) using propofol was carried out on all participants in which the real-time site of obstruction and frequency of snoring were recorded. The frequency spectra of snores at the respective level of obstruction were documented.
Results: Most participants (62.5%) in this study were found to have multi-level obstruction and the commonest was palate and oropharynx (52.5%) in which bi-peak frequency was detected with mean of 463.68Hz and 1086.96Hz. The median peak frequency of palatal, oropharynx and epiglottis snoring was 522.5Hz, 482.4Hz and 300.0Hz respectively. The severity of AHI was significantly associated with multi-level obstruction ($p<0.0001$). There was no significant difference between the mean frequency of snoring during natural sleep and induced sleep.
Conclusion: This study documented bi-peak snore frequency in multilevel obstruction and uni-peak frequency in uni-level obstruction. Multilevel airway obstruction during sleep was associated with more severe OSA. The snore frequency recorded during induced sleep was representative of natural sleep.

Oral

PERCEIVED BARRIERS TO IMPROVE PHYSICAL ACTIVITY AND DIETARY INTAKE AMONG OVERWEIGHT AND OBESE WORKERS IN A WORKPLACE WELLNESS PROGRAMME

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Introduction: Workplace wellness programmes are a public health strategy to address the rising obesity trend globally. The 'Healthy Worker Programme' is a 6-month worksite intervention among 132 overweight and obese workers to promote weight management at a government office in Kuala Lumpur. It is important to understand perceived barriers by participants, which can reduce their success in weight loss.
O**bjective:** To determine barriers perceived by participants of the "Healthy Worker Programme" to improve their physical activity and dietary intake.
Methods: A qualitative inquiry using in-depth interviews were conducted on programme participants from different backgrounds (such as age, sex, race and marital status), until saturation point. Data was coded and thematic analysis was undertaken.
Results: Saturation point occurred by the tenth interview. Perceived barriers were environmental exposures (such as exposures to unhealthy foods at work, home and at social events), health conditions, poor knowledge on how to reduce weight through dietary changes and psychological barriers, such as low motivation and lack of discipline.
Conclusion: Understanding barriers perceived by participants of a workplace wellness programme can help programme coordinators to improve it. The "Healthy Worker Programme" can be further improved, such as by increasing the workers' motivation through regular talks or counseling and more education on how to eat healthily and low-impact exercises for those with health conditions.

Oral

EPIGENOME ANALYSIS OF COLORECTAL CANCER: A GENOME WIDE APPROACH

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Introduction: Malaysia incidence rate of CRC is 21.3 cases per 100,000 population. Many molecular pathways are involved in carcinogenesis including DNA methylation. Genes with high levels of 5-methylcytosine (hypermethylation) in the promoter regions are associated with gene silencing and may alter the signalling pathway that contribute to CRC tumorigenesis. On the other hand, genes with low levels of 5-methylcytosine (hypomethylation) have also been implicated in CRC progression through tumor-suppressor genes or act as oncogenes.
Objective: To comprehensively characterize the differentially methylated regions involved in CRC pathogenesis.
Methods: Genomic DNA was extracted from 12 paired matched samples collected from UKM Medical Centre (UKMMC). Bisulfite conversion was performed and the bisulfite converted DNA was subjected to microarray using Human Infinium Epic Beadchip Array. The data was analyzed using Partek Genomic Suite 6.6.and David Bioinformatics Resources 6.8.
Results: There were 25,377 genes significantly differentially methylated on CpG loci ($p \leq 0.05$), with 10,573 hypermethylated and 14,804 hypomethylated genes. Pathway enrichment analysis revealed involvement of 743 genes in the colorectal cancer pathway, 451 genes in MAPK signalling and 208 genes in Wnt signalling pathway. By overlapping these three different pathways, 30 hyper- and hypomethylated genes were identified. *MAPK9, RAC1* and *PRKACA* are top three hypermethylated genes whereas *MYC, PRKACB* and *PRKCG* are the top three hypomethylated genes.
Conclusion: This is the first look at the methylation profile of local CRC patients using the latest platform assay. The new knowledge from this study can be utilized for personalized health diagnostics, disease prediction, and monitoring of treatment.

Oral

OXIDATIVE STRESS GENE MUTATIONS IN FAMILIAL HYPERCHOLESTEROLEMIA (FH) PATIENTS

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Introduction: Oxidative stress is an important inducer of many diseases including cardiovascular diseases (CVD). Hypercholesterolemia is one of the key contributors to CVD which are the leading cause of mortality worldwide. Familial hypercholesterolemia (FH) is an autosomal dominant disease involving lipid metabolism.
Objective: We aimed to determine the oxidative stress gene mutations in FH patients. The possible pathway involved in the development of CVD was also identified.
Methods: The study design was a case-control with purposive sampling and participants were recruited from The Malaysian Cohort (TMC) project. Extreme group comparison was used to select 25 individuals with high and low total cholesterol and low-density lipoprotein-cholesterol DNA was extracted and whole exome sequencing was performed using the Ion Proton. All variants were annotated and filtered using ANNOVAR. Variants were cross-referenced against the publicly available databases. In total, 295 genes involved in the oxidative stress pathways were included.
Results: There are 10 genes that are unique for FH patients (*PRKAA2, PRLCB, IL6, MT3, MPV, MB, GAPDH, DHCR24, APOA1* and *ADIPOQ*). 4 samples (H14, H15, H16 and H21) have several mutations in the oxidative stress genes as well as in the lipid metabolism genes H15 and H21 have family history of CVD.
Conclusion: The AGE-RAGE signalling pathway which plays a role in the age-related diseases was associated with CVD in these FH patients. Identification of mutations in the oxidative stress pathway among FH patients may predict the risk of cardiovascular disease (CVD) in the future.

Oral

ASSOCIATION BETWEEN *TNF* POLYMORPHISMS AND RISK OF HPV-MEDIATED CERVICAL CANCER AMONG MALAYSIAN WOMEN

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Introduction: Human papillomavirus (HPV) is the central etiological agent of cervical cancer. However, HPV infection alone is insufficient to result in carcinogenesis. Genetic factors are equally important in determining the disease progression. Tumor necrosis factor (TNF) is a pleiotropic cytokine which has been implicated in tumor development and progression. Polymorphisms in *TNF* gene could potentially affect the level (and thus, function) of the cytokine, which could in turn, influence cervical cancer risk.
Objective: To investigate the allele and genotype frequencies and the association of *TNF* -238G>A (rs361525) and -308G>A (rs1800629) polymorphisms with the risk of cervical cancer among Malaysian women.
Methods: A total of 154 histopathologically-confirmed cervical cancer patients and 209 cancer-free healthy female controls were recruited. The polymorphisms were genotyped on the genomic DNA of the subjects by using PCR-RFLP method, and confirmed by DNA sequencing. Logistic regression analysis was performed to examine the association between the polymorphisms and cervical cancer risk.
Results: After adjustment for potential confounders, statistically significant association was observed only for the -308G>A polymorphism. The heterozygous (GA) genotype of the polymorphism was associated with a 1.591-fold increased risk of cervical cancer (95% CI=1.034-2.448, P=0.035), while the homozygous variant (AA) genotype had an adjusted odds ratio (aOR) of 3.471 (95% CI=1.545-7.795, P=0.003). At the allelic level, the variant (A) allele was also associated with an increased cervical cancer risk, with aOR=1.801 (95% CI=1.295-2.505, P<0.001).
Conclusion: The *TNF*-308G>A polymorphism, but not the -238G>A polymorphism, was associated with an increased risk of cervical cancer among Malaysian women.

Oral

SECRETORY PHOSPHOLIPASE A2 GROUP IIA (SPLA2-IIA) TRIGGERS EICOSANOID PATHWAY IN BACTERIAL SEPSIS MODEL USING U937 CELL

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Introduction: Bacterial sepsis involves complex sequence of inflammatory events following infection. Elevation of secretory phospholipase A2 Group IIA (sPLA2-IIA) and eicosanoid metabolites levels in blood has been reported separately in the condition of bacterial sepsis.
Objective: The aim of this study was to determine the mechanism of sPLA2-IIA in eicosanoid pathway using human monocytic cell line U937.
Methods: U937 cells were treated with lipopolysaccharide (LPS) or exogenous sPLA2-IIA. The effect of exogenous sPLA2-IIA on cells proliferation rate was measured by MTS assay; meanwhile nitric oxide production, cyclooxygenase enzymes (COX-1 & COX-2) activities and NF-κB activation were measured using ELISA kits.
Results: A decrease in the proliferation rate of U937 cells was observed (<20%; $p<0.05$). Cells treated with LPS augmented nitric oxide and COX-2 activities through NF-κB activation ($p<0.05$). Similarly, cells treated with sPLA2-IIA augmented nitric oxide and COX-2 activities, but not via NF-κB activation.
Conclusion: U937 cells treated with sPLA2-IIA triggers inflammation but not via activation of NF-κB. This bacterial sepsis cell model suggests that sPLA2-IIA may play a complementary role in the complex sepsis inflammatory cascade in human.

Poster

KNOWLEDGE, ATTITUDE AND PRACTICE REGARDING OSTEOPOROSIS AND METABOLIC DISEASES AMONG MIDDLE AGE AND ELDERLY POPULATION

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Introduction: Osteoporosis and metabolic diseases, namely hypertension and diabetes mellitus, are lifestyle preventable diseases that have high prevalence amongst the middle-aged and elderly populations. The awareness on these diseases of the general population in these age group in the rural and urban sites in Malaysia are uncertain.
Objective: This study aimed to determine the knowledge, attitude and practice (KAP) of osteoporosis and metabolic diseases, amongst middle-aged and elderly general population in rural and urban states.
Methods: A cross-sectional study via researcher-assisted KAP questionnaire was carried out in 350 respondents aged 45 years old and above in two states, namely Perlis and Kuala Lumpur. Random and convenient samplings were used for the selection and recruitment of apparently healthy subjects from the community and institutional settings.
Results: In general, more than half of the correspondents (66.3%) had good knowledge on osteoporosis and metabolic diseases with more than 70% of correct answers. Majority of the study participants (85.7%) had positive attitude healthy lifestyle behaviors to prevent themselves from these diseases but only half of them (43.1%) practiced these positive activities. The KAP score is higher in female gender, Chinese ethnicity, non-working individuals, and individuals with diagnosed osteoporosis and metabolic diseases ($p<0.05$). Geographical differences reflecting urban and rural populations produced differential scores in the practice component whereby the rural (Perlis) population had a higher score ($p<0.005$).
Conclusion: Despite relatively good knowledge and attitude amongst Malaysian, there is still a gap in translating these into actual disease preventing activities.

Poster

TO STUDY THE EXPRESSION OF STAT6 IN SOLITARY FIBROUS TUMOUR

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Introduction: Solitary fibrous tumour (SFT) is a fibrotic neoplasm, also previously designated as hemangiopericytoma. STAT6 is a protein for signal tranducers and activators of transcription (STAT) family which involved in immune function and early cell growth. Oncogenic alteration of STAT6 plays important role for specific driver for tumour genesis of solitary fibrous tumour via NAB2-STAT6 fusion gene. The aim of the study was to compare and evaluate STAT6 expression between SFT and other soft tissue histological mimics.
Material and Methods: We evaluated a total of 30 cases material formalin fixed paraffin embedded tissue block previously diagnosed SFT cases (n=14) and soft tissue tumours mimic cases (n=16) over period of 15 years.
Results: Fourteen SFT cases (100%) showed nuclear expression of STAT6, which was diffuse and intense. All other tumour types were negative for STAT6, except for one case of dedifferentiated liposarcoma, one gastrointestinal stromal tumour and one spindle cell lipoma which showed weak non-specific cytoplasmic staining.
Conclusion: Nuclear STAT6 expression is useful and reliable as adjunctive marker for solitary fibrous tumour when the diagnosis is inconclusive by conventional methods.

Keywords: Solitary fibrous tumour (SFT), hemangiopericytoma, immunohistochemistry, STAT6, histological mimics

Poster

A STUDY ON THE APPROPRIATENESS OF EARLY EMPIRICAL ANTIBIOTIC THERAPY ASSOCIATION WITH 28-DAY MORTALITY AMONG PATIENTS WITH SEPSIS SYNDROME PRESENTED TO EMERGENCY DEPARTMENT IN UKMMC

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Introduction: The mortality rate for sepsis is high and it has been widely researched to discover the methods for effective sepsis management. Early treatment with appropriate antibiotic should reduce mortality.
Objective: To determine the association of early appropriate antibiotic administration and 28-day mortality in sepsis syndrome patient presented in Emergency Department (ED) Universiti Kebangsaan Malaysia Medical Centre (UKMMC).
Methods: This is a single-centre retrospective cross-sectional study in ED UKMMC, with patients aged 18 years and older with signs of systemic inflammatory response syndrome, suspected infection and administered antibiotics. All available culture and sensitivity results were trace. Patients were followed up on 28-day mortality for outcome and were compared on time and appropriateness of antibiotics given.
Results: 519 cases were included into the study. There were 472 (90.9%) survivors and 47 (9.1%) non-survivors for 28-day mortality. Early (within 6 hours upon arrival in ED) and late (more than 6 hours) administration of antibiotics have significant associations with 28-day mortality ($p<0.001$). However, appropriateness (according to culture and sensitivity or UKMMC antibiotic protocol) of antibiotic administered have no associations with 28-day mortality ($p = 0.099$).
Conclusions: Timing of antibiotics given to sepsis patients is important. The antibiotic was given early as per protocol. The early administration of empirical antibiotic was significantly associated with 28-day mortality. This signifies that the administration of early empirical antibiotic could reduce mortality in ED PPUKM. Nevertheless, the study was unable to demonstrate the appropriateness of antibiotics given to patient improve 28-day mortality in sepsis patients.

Poster

INTERLEUKIN 1β LEVEL IN ACQUIRED LARYNGOTRACHEAL STENOSIS PATIENTS IN UNIVERSITY KEBANGSAAN MALAYSIA MEDICAL CENTRE: PRELIMINARY RESULTS

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Introduction: Acquired laryngotracheal stenosis (ALTS) remains one of the most challenging problems in otolaryngology and Interleukin-1beta (IL-1β) has been identified as the main inflammatory mediator.
Objective: To determine the trend of IL-1β levels in the blood of adults ALTS patients.
Materials and Methods: 13 participants with ALTS (10 severe and 3 mild stenosis) and 5 healthy volunteers were recruited from UKMMC-ORL clinic. The grade of stenosis was documented and blood samples taken at four different time intervals of 6-12 weeks with the IL-1β level determined by performing ELISA tests. The IL-1βlevel was compared between: severe ALTS and healthy; severe and mild ALTS. The trend of IL-1β level was compared with the severity of stenosis.
Results: Severe ALTS patients before intervention showed significantly higher level of IL-1β compared to healthy volunteers (p=0.005). Severe ALTS patients before intervention had higher IL-1β level compared to severe ALTS patients after interventions (p=0.0009). The mean of IL-1β of severe ALTS patients was higher than the mild ALTS patients throughout this study period. Due to wide variation in IL-1β level of severe ALTS patients, the difference was not statistically significant. The IL-1β level showed reducing trend with the improvement of the Cotton Myer grading of stenosis for patients who underwent open surgery or ELLS who managed to be decannulated.
Conclusion: IL-1β is associated with ALTS severity and is higher in the ALTS group than the healthy group. These findings provide a baseline for further research in ALTS that may help the management and treatment.

Keywords: Acquired laryngotracheal stenosis (ALTS), Interleukin-1beta (IL-1β),

Laryngeal Stenosis

Poster

DIFFERENT VIABILITY RESPONSE ON ANTIOXIDANT AND OXIDANT EXPOSURE IN AUTISM LYMPHOBLASTOID CELL LINES WITH THE NON-AUTISTIC SIBLING

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Introduction: Autism Spectrum Disorder is a neurodevelopmental condition which is associated with oxidative imbalance between oxidant and antioxidant. It has been proven that Tocotrienol-rich Fraction (TRF) has antioxidant properties by *in vitro* and *in vivo* studies.
Objective: To determine the effect of TRF and hydrogen peroxide (H_2O_2) on the viability of cells after induced to ALCLs and NALCLs.
Methods: In this study, a single pair of Lymphoblastoid Cell Lines (LCLs) from children with autism (ALCLs) and their non-autistic (NALCLs) sibling were used and cultured. Cells were divided into 4 groups: cells treated with TRF, H_2O_2, pre-treatment (TRF and H_2O_2), and post-treatment (H_2O_2 - TRF). Cells were incubated with antioxidant containing medium, TRF for 24 h and H_2O_2 for 1 h.
Results: The viability test on ALCLs showed that the proliferation of ALCLs was increased at 8 µg/ml TRF (P = 0.009) compared to untreated control. However, there was no significant effect on the viability of the NALCLs after treated with TRF. On the other hand, the H_2O_2 reduced the proliferation of the ALCLs and the NALCLs with the same IC50 at 150 µM (47%, P = 0.009).
Conclusion: These findings suggested that TRF exhibited selective effect on ALCLs with positive response in increasing the viability of cells while no effect was seen on the normal cells. TRF might restore the antioxidant activity in ALCLs thus increasing the proliferation capacity of the cells. Amount of H_2O_2 exposure to both of cells imposed the same oxidative stress response that caused the decreased in proliferation that might be due to apoptosis, necrosis or growth arrest.

Poster

POLYMORPHISMS IN *CCND1* GENE AND THEIR INFLUENCE ON THE RISK OF CERVICAL CANCER IN MALAYSIAN POPULATION

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Introduction: Human papillomavirus (HPV) is an essential, but not sufficient, cause of cervical cancer. Genetic factors involved in major cellular processes, such as cell cycle regulation, play an important role in determining the fate of HPV-infected cells. Cyclin D1, encoded by the *CCND1* gene, is a key coordinator of the G1-to-S phase transition of the cell cycle. Polymorphisms in *CCND1* gene could affect the function of the protein product, and may consequently influence cervical cancer risk.
Objective: To investigate the allele and genotype frequencies and the association of *CCND1* 870G>A and 1722C>G polymorphisms with the risk of cervical cancer in the Malaysian population.
Methods: The polymorphisms were genotyped on 154 cervical cancer patients and 209 cancer-free healthy female controls via PCR-RFLP technique, followed by DNA sequencing. The odds ratios (ORs) were derived from a logistic regression model and adjusted for potential confounders to assess the relationship between the polymorphisms and cervical cancer risk.
Results: The heterozygous genotype of the *CCND1* 870G>A polymorphism was found to be significantly associated with a decreased cervical cancer risk, with an adjusted OR of 0.434 (95% CI=0.257-0.732, P=0.002). However, significant association was not observed for the homozygous variant genotype as well as the variant allele (P>0.05). On the other hand, for the *CCND1* 1722C>G polymorphism, no significant association was noted for the heterozygous genotype, homozygous variant genotype and the variant allele (P>0.05).

Conclusion: The heterozygous genotype of the *CCND1* 870G>A polymorphism was significantly associated with a reduced risk of cervical cancer in the Malaysian population.

Poster

ASSOCIATION OF SINGLE NUCLEOTIDE POLYMORPHISMS (SNPs) of *CYP11B2, CYP11B1* AND *CYP17A1* WITH PRIMARY ALDOSTERONISM IN A MULTIETHNIC MALAYSIA COHORT

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Introduction: Primary aldosteronism (PA), also known as Conn's syndrome, is a common curable cause of hypertension. Familial studies of essential hypertensive patients suggest that heritable genetic factors play a role in blood pressure regulation. Interestingly, single nucleotide polymorphisms (SNP) in genes encoding enzymes involved in adrenal steroidogenesis, CYP11B2, CYP11B1 and CYP17A1, are associated with increased risk of hypertension. Therefore, we analysed selected SNPs in these genes to determine their associations with PA.
Methods: We performed an association study for selected SNPs of the steroidogenic enzyme genes CYP11B2 (rs4546 and rs1799998), CYP11B1 (rs6410), and CYP17A1 (rs1004467) in a PA population using TaqMan Genotyping assays on the ABI 7000 Sequence Detection System. Genotyping was performed on 40-50 PA patients and a similar number of non-hypertensive healthy individuals. Case-control genetic association analysis was performed at http://www.oege.org/software/orcalc.html.
Results: Minor allele frequencies (MAF) across the 4 SNPs studied were similar to those reported in other Asian populations but significantly different from European populations (rs4546 MAF: A=0.369/68, rs1799998 MAF: G=0.276/48, rs6410 MAF: T=0.298/40, rs1004467 MAF: G=0.224/53). Minor allele homozygotes for rs4546 had significantly increased risk of PA compared to heterozygotes (OR: Infinity, 95% CI: NaN-Infinity, p=0.041). Individuals heterozygous for rs4546 showed a highly significant (p=0.011) reduced PA risk relative to major allele homozygotes (OR:0.24, 95% CI: 0.08-0.75).
Conclusion: The CYP11B2 rs4546 SNP associates with PA in our Asian population. However, more functional experiments need to be performed to find out whether this SNP is causal for PA or whether it is in linkage disequilibrium with the actual functional causative SNP. Once functional SNP is known, identification of these germline variants in asymptomatic family members would allow early screening of PA to be offered and potentially provide novel drug targets to treat the disease.

Poster

ASSOCIATION BETWEEN 6-TGN LEVELS AND REMISSION OF IBD IN ASIAN PATIENTS: A META-ANALYSIS

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Introduction: Thiopurine compounds, azathioprine and 6-mercaptopurine are important modalities in the therapy of inflammatory bowel disease (IBD). The serum level of an active thiopurine metabolite, 6-thioguanine nucleotide (6-TGN), is a marker of treatment efficacy. However, the utility of 6-TGN testing has yet to be confirmed in Asian IBD patients.
Objective: We aimed to examine the use of 6-TGN levels to predict remission of IBD in Asian patients.
Methods: We performed a systematic literature search in three databases to identify eligible studies. We then conducted a two-part meta-analysis to ascertain the association of 6-TGN levels with IBD remission.
Results: Six studies defined a target threshold (>225 or 235 pmol/8 x 10^8 RBCs) for predicting disease remission; another overlapping set of five studies reported mean 6-TGN levels alongside remission status. Overall, Asian IBD patients were more likely to attain disease remission when their 6-TGN levels exceeded 225 or 235 pmol/8 10^8 RBCs (pooled OR=2.51; 95% CI, 1.42-4.45; p=0.002). Also, we noted that mean 6-TGN levels were substantially higher in patients with quiescent IBD than those with active disease (pooled difference=74.59 pmol/8 x 10^8 RBCs; 95% CI, 31.53-117.65; p=0.0007).
Conclusions: We have demonstrated a positive correlation between 6-TGN levels and the outcome of IBD treatment in Asian patients. However, two major sources of between-study heterogeneity were detected, namely the methodology of 6-TGN measurement and age-related differences in thiopurine disposition. Routine, pre-treatment 6-TGN testing may be recommended for Asian IBD patients, but a standard analytical procedure needs to be first established.

Poster

INCREASED MITOCHONDRIAL FUNCTION IN AUTISM LYMPHOBLASTOID CELL LINE COMPARED TO NON-AUTISM CELL

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Introduction: Autism spectrum disorder (ASD) is characterised by lasting problems with social communication and social interaction, restricted and repetitive behaviours, and symptoms become apparent only at the age of 2. Recently, mitochondrial dysfunction (mtD) has been proposed to explain the connection between the diverse medical symptoms associated with ASDs. Currently it is believed that mtD may be present in up to 80% of children with ASD and around 5 to 10 percent of children with autism have mtD as the underlying cause of their symptoms.
Objective: This study aimed to compare the mitochondrial function between autism lymphoblastoid cell line (ALCL) and non-autism cell line (NALCL).
Methods: The mitochondrial function and respiration of the lymphoblastoid cell line was performed using a modular instrument for high-resolution respirometry, Oxygraph-2k (O2k).
Results: Our results showed that the OXPHOS capacity (P) and ETS capacity (E) in ALCL is significantly higher compared to NALCL ($p<0.01$). In an experiment measuring the CII-linked respiration rate and mitochondrial membrane potential (MMP) simultaneously, the CII-linked P and E are higher in ALCL compared to NALCL ($p<0.01$) although MMP does not show significant difference between the two states of respiration. In addition, complex IV activity was found to be higher in ALCL as compared to NALCL ($p<01$).
Conclusion: In conclusion, the overall activity in the pathway generating ATP in ALCL is higher than in NALCL except for the MMP leading to the mtD.

Poster

TESTOSTERONE REDUCES EXPRESSION OF CLAUDIN-4 AND OCCLUDIN IN THE ENDOMETRIUM DURING THE PERIOD OF UTERINE RECEPTIVITY IN RATS

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Introduction: Implantation is a highly controlled process that regulates interaction between the blastocyst and the receptive endometrium. Disturbances in the fluid environment and expression of endometrial proteins during uterine receptivity period may lead to failure of embryo implantation. Testosterone has been reported to affect the fluid transport and other events during embryo implantation.
Objective: This study aimed to investigate the effects of testosterone on the expression of claudin-4 and occludin in the uterus during uterine receptivity.
Methods: Ovariectomized adult female rats received 8 days of sex-steroid replacement regimes intended to mimic hormonal changes in early pregnancy. Testosterone (1mg/kg/day) was given either alone or in combination with flutamide or finasteride between days 6 to 8, which was considered as the period of uterine receptivity. At the end of the treatment, rats were sacrificed and uteri were removed. Expression and distribution of claudin-4 and occludin were examined by Western blotting and immunoflourescence (IF) respectively.
Results: Increased expression of claudin-4 and occludin were observed in rats receiving normal sex-steroid replacement regime. Administration of testosterone during uterine receptivity period resulted in reduced expressions of claudin-4 and occludin. Testosterone effects were not antagonized either by flutamide or finasteride.
Conclusions: Decreased in expressions of claudin-4 and occludin during the period of uterine receptivity by testosterone may interfere with embryo implantation in situation associated with high level of this hormone.

Poster

HOT WATER EXTRACT OF *SACCHAROMYCES CEREVISIAE* ENHIBITS ANTIOXIDANT ACTICITY

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Introduction: The free radical theory of aging identifies the accumulation of reactive oxygen species (ROS) as a cause that leads to oxidative stress and aging. Studies have shown that compounds and extracts exhibiting antioxidant activity ameliorate the debilitating effects of oxidative stress. Extracts from the yeast *Saccharomyces cerevisiae* have been reported to have antioxidant effect. This study focuses on optimising yeast extract preparation, in which the extract can be used in future studies.
Objective: This study aimed to determine the optimum extraction method, and the optimum harvesting time of *S. cerevisiae* culture; to obtain the highest antioxidant activity.
Methods: Two extraction methods were carried out. Method 1: Cells were boiled at 100˚C for 20 mins and centrifuged; followed by collection of the the supernatant that contained the extract. Method 2: Cells were centrifuged at 4˚C for 13 mins for lysis, followed by the collection of the supernatant. Extracts from both methods were subjected to DPPH assay to measure the antioxidant activity. Cultures were also harvested hourly up to 15 hours. Extracts at each hour were prepared by method 1 and subjected to DPPH assay.
Results: Method 1 produced the highest antioxidant activity compared to method 2. Cells grown for 3 hours produced extract with the highest antioxidant activity.
Conclusion: Hot water extraction (100˚C) produced the highest antioxidant activity inyeast extract from cells grown for 3 hours.

Poster

APPLICATION OF INTERPHASE FLUORESCENCE IN SITU HYBRIDIZATION (iFISH) FOR THE DETECTION OF CHROMOSOME ABNORMALITIES IN ACUTE LYMPHOBLASTIC LUEKAEMIA

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Introduction: Acute Lymphoblastic Leukemia (ALL) is a malignant disease of the bone marrow in which early lymphoid precursors proliferate and replace the normal hematopoietic cells of the marrow. Cytogenetic analysis of leukemic blasts plays an important role in classification and prognosis in ALL patients.
Objective: This study was carried out to demonstrate the importance of interphase fluorescence in situ hybridization (iFISH) for the detection of chromosomal abnormalities in ALL.
Methods: This is a retrospective study of ALL cases which were analysed in the Cytogenetic Unit, UKMMC from January 2012 until April 2018. The ALL panel probes used include Vysis LSI BCR/ABL Dual Color Dual Fusion Translocation Probe, Vysis LSI ETV6/RUNX1 ES Dual Color Translocation Probe, Vysis LSI TCF3/PBX1 Dual Color, Dual Fusion Translocation Probe and Vysis LSI MLL Dual Color, Break Apart Rearrangement Probe. At least 200 nuclei were analysed in each case.
Results: A total of 67 cases were analysed, of which 30(~45%) were successfully karyotyped while the remaining 37(~55%) showed no metaphase or poor chromosome morphology. iFISH performed on the cases showed various abnormalities: t(12;21)(p13;q22) [ETV6-RUNX1], t(9;22)(q34;q11.2) [BCR-ABL], t(1;19)(q23;p13)[PBX1-TCF3] and MLL (11q23) rearrangement.
Conclusion: iFISH is a reliable method for identification of submicroscopic chromosomal abnormalities in ALL.

Poster

EVIDENCE OF CLONAL REPLACEMENT OF METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA) STRAINS IN UKM MEDICAL CENTRE: A PRELIMINARY OBSERVATION

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Introduction: Surveillance molecular typing of methicillin-resistant *Staphylococcus aureus* (MRSA) strains isolated from hospital settings is important to understand the pathogen's transmission dynamics and its temporal genetic shifts.
Methods: This study is a preliminary observation on the molecular genotypes of MRSA strains isolated in January, 2009 and January, 2018, from various wards of UKM Medical Centre. SCC*mec* and staphylococcal enterotoxin gene typing was carried out on MRSAs isolated during the study period via PCR and gel electrophoresis.
Results: A total of 23 and 33 MRSA strains were isolated in the month of January, 2009 and January 2018, respectively. Interestingly, even though most of the strains (n = 19, 82.6%) isolated in January, 2009 were of SCC*mec* type III-SCCmercury with *ccrC*, a genetic shift of the strains was observed in January, 2018, whereby 97.0% (n = 32) strains were typed as SCC*mec* type IV. In addition, enterotoxin gene profile of the strains has also evolved in January, 2018 compared to January, 2009. While most strains (n = 18, 78.3%) isolated in January, 2009 harboured only the staphylococcal enterotoxin A gene (*sea*), almost all strains (n = 31, 93.9%) isolated in January, 2018 carried the *seg* and *sei* genes, but not *sea*.
Conclusion: Results from this preliminary observation shows evidence of MRSA clonal replacement in UKM Medical Centre. The dominant MRSA clone from this medical centre has shifted from a hospital-associated genotype (SCC*mec* type III) in 2009 to a fitter, community-associated genotype (SCC*mec* type IV) isolated in 2018. Clinical importance of this clonal replacement is currently being investigated.

Poster

KELULUT HONEY IMPROVES FASTING BLOOD GLUCOSE AND LIPID PROFILE ON METABOLIC SYNDROME-INDUCED RATS

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Introduction: Herbs and plant-based food supplements have been used for centuries as part of complementary medicine. Honey for example, is not only known for its nutritional benefit but also as traditional medicine due to its healing properties. It has been proven that honey exert antioxidant, anti-inflammatory, anti-bacterial and anti-mutagenic properties. Over the past few years, there has been surge of interest in the ability of honey as antioxidant followed by its protective effects on the brain and other organs.
Objective: The aim of this study is to determine the effects of Kelulut honey on fasting blood profile of the Metabolic Syndrome (MetS)-induced rats.
Methods: Twenty-four Wistar male rats were divided into 3 groups; Control 16-weeks (C16) group, 16-weeks of HCHF diet (MetS16) group and 16-weeks of HCHF diet and received Kelulut honey supplementation (KH) group. After the given period, their fasting blood glucose, lipid profile and blood pressure were measured.
Results: Kelulut honey supplementation for 35 days was found to decrease the fasting blood glucose level significantly in the KH group ($p<0.05$) as compared to the MetS16 group. Total cholesterol and low density lipoprotein (LDL) level in the KH group were also significantly reduced ($p<0.05$) when compared to the C16 group. Systolic blood pressure was significantly reduced in KH group ($p<0.05$) than the MetS16 group, but no significant difference was observed on the diastolic blood pressure.
Conclusion: Kelulut honey supplementation was shown to improve fasting blood glucose, reduce the LDL level, and maintain the HDL level. It also helps to maintain normal blood pressure. Kelulut honey may be a beneficial supplementation in patient with MetS especially during its early phase.

Poster

CIRCULATING hsa-miR-17-3p AS A POTENTIAL BIOMARKER FOR PRE-SYMPTOMATIC COLORECTAL CANCER

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Introduction: Colorectal cancer (CRC) is the second leading cancer in Malaysia and is mostly asymptomatic at early stages. Early detection biomarkers are needed to improve survival. Circulating microRNAs play a significant role in carcinogenesis and have been proposed as biomarkers for cancer screening.
Objective: To identify microRNA(s) that could serve as biomarkers of cancer predisposition and for early detection of CRC.
Methods: MicroRNAs were isolated from 50 µL of serum taken at the presymptomatic stage from 5 participants of The Malaysian Cohort project during recruitment, who had eventually died of colorectal cancer. Another 5 individuals who did not develop any cancer after five years were used as controls. cDNA was synthesized and used for real-time PCR containing a panel of 84 most important microRNAs associated with human serum. The fold change was analysed using $2^{-\Delta\Delta Ct}$ method and T test was utilized to determine the significant differences between two groups.
Results: Using 1.5-fold as a cutoff for expression regulation, 13 microRNAs exhibited differential expression. Upon applying a p-value of <0.05, hsa-miR-17-3p expression (-2.9644 fold) was found to be significantly down-regulated with a p value of 0.0395. Pathway and target prediction analysis of hsa-miR-17-3p revealed significant enrichment of 24 KEGG pathways, with pathways in cancer, proteoglycans in cancer and focal adhesion pathways containing the highest number of genes targeted by this microRNA.
Conclusion: The involvement of hsa-miR-17-3p in these pathways warrants further investigation in the search of biomarker for pre-symptomatic of CRC.

Poster

OTOLOGICAL AND AUDIOLOGICAL MANIFESTATIONS AMONG CHILDREN WITH DOWN SYNDROME IN UKMMC

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Introduction: Otological and audiological manifestations in Down Syndrome (DS) individuals are important features documented in literature. DS is associated with high prevalence of hearing loss indicateing that interventions need to be advocated to improve the quality of life of DS individuals.
Objective: To investigate hearing loss, and audiological data among children with DS.
Methods: A cross sectional study was initiated in year 2017 at the UKM Medical Centre, among 67 children with DS who fulfilled the criteria. Otological features including pinna features, otoscopic findings, hearing assessment and audiological profiles were documented and evaluated. Descriptive analysis has been performed.
Results: Majority of children with DS have low set ears (67%) and small pinna (73. Half of them have cerumen obstruction in the ear canal, 80% had intact tympanic membrane. High prevalence of hearing loss are documented, 71.6% by subjects and 66.4% by ears tested. Among the subjects with hearing loss, 81% had bilateral hearing loss. The most common type is conductive hearing loss, while mild to moderate hearing loss are the most common manifestation observed. 59% have tympanogram type B suggestive of middle ear effusion.
Conclusion: There is a high prevalence of hearing loss in children with DS, with conductive type being the most common, and the degree suffered mostly mild and moderate.

Poster

PREOPERATIVE OPTICAL COHERENCE TOMOGRAPHY ASSESSMENT OF IDIOPATHIC FULL THICKNESS MACULAR HOLE: PREDICTING MORPHOLOGICAL AND VISUAL OUTCOME

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Objective: To compare the predictive capability of several preoperative OCT measurements of idiopathic full thickness macular hole.
Design: Prospective study.
Participants: A total of 40 patients who consented for macula hole surgery.
Methods: All patients were screened to exclude other causes of maculopathy, followed by metamorphopsia questionnaire, refraction test and macula SD-OCT measurements before and at 3 months post-operative.
Outcome Measures: OCT macula hole measurement, corrected visual acuity and metamorphopsia score.
Result: The subjects age ranged between 39 to 80 years with a mean (SD) age of 62.4 (±8.6) years. Slightly more than half of them (55%) had symptoms for more than 6 months, 20% presented symptoms within the first 6 months whereas another 25% had unclear duration of symptoms by history. 12 (30%) subjects had stage 2 macular hole while 28 (70%) were at stage 3 and 4. The baseline pre-operative BCVA was logMAR 1.30 (0.53) (equivalent to 6/120 on the snellen chart). Following macular hole surgery, 90% achieved anatomical closure either type 1 or type 2 closure, 70% gain visual acuity of 2 lines or more with subjective improvement of metamorphopsia. Pre-operative base diameter and MHI showed weak correlation with post-operative visual acuity at 3 months. Meanwhile none of the OCT parameter and indexes demonstrates their predictive capability for post-operative MH closure at 3 months.
Conclusion: The morphological and visual outcome of macular hole surgery is doubtless. Besides pre-operative OCT assessment of MH, confounding factors including age, duration of symptoms, baseline visual acuity should be considered for prognostication.

Poster

Local Anaesthesia Systemic Toxicity (LAST) – A Stroke Mimicker

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Introduction: Local anaesthesia systemic toxicity (LAST) is uncommon. It may be affected by the choice of drug, the administration technique or the patient. Incidence of LAST for peripheral nerve block was 9.8 per 10,000.

Case report: A 55 years-old lady presented to Emergency Department (ED) with dizziness, numbness of tongue and mouth, progressively developed slurring of speech and quadriplegia. She developed symptoms after 10 minutes of intra-articular injection to the right shoulder with the mixture of 2% lignocaine (200mg) and hydrocortisone (1ml) for her supraspinatus tendinopathy at orthopaedic clinic. In ED, she was conscious but had significant slurring of speech, unable to open eyes and mouth. Both pupils were reactive. Neurological examination revealed hypotonia, power 0/5 but normal reflexes for all four limbs. There was marked reduce sensation over face. Cardiorespiratory function was stable. Electrocardiogram showed no arrhythmia. There was no documented hypoxia. An urgent head CT scan & spine MRI showed no abnormality. She was admitted for supportive care. Her slurring of speech resolved after six hours and full recovery of neurological function over nine days.

Discussion: Rapid central neural blockade may happen during intra-articular shoulder injection. It may be due to accidentally injection of local anaesthetic in the dural cuff which travel retrogradely into subepineural space and later into spinal cord. Prolonged block is likely due to slow spread of drug through epidural fat to intradural space.

Conclusion: Intra-articular injection in shoulder may cause LAST which may be under recognized as it can mimic stroke.

Poster

A CASE OF PARAGANGLIOMA WITH SYANOTIC CONGENITAL HEART DISEASE

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We reported a case of left paraganglioma (PGL) in a 20 years old lady with underlying complicated cyanotic heart disease since birth and had undergone palliative Glenn shunt, with history of cavernous sinus thrombosis. She presented with symptoms of PGL with no family history of malignancy. Clinically she is hypertensive, cyanosis with clinical evidence of pulmonary hypertension. 24 hours urine noradrenaline was 548.2 microgram/day (six times above normal range) and contrasted enhanced computed tomography (CECT) neck, thorax, abdomen and pelvis showed enhancing left paraaortic mass sized 5.2cm x 4.4cm x 3.8cm. A diagnosis of left PGL was made. She was admitted for blood pressure control with selective alpha-1 inhibitors and beta-blockers. Surgical intervention was unable to proceed due to high risk procedure. Currently, she is still under our care for blood pressure management and 6 monthly CECT scan monitoring. In conclusion, there is reported association of PGL with cyanotic congenital heart disease although the exact mechanism is still unclear. Her chronic hypoxia since birth likely contributed to the development of PGL. Thus, early screening must be consider in this group of patients. There is still no definite medical therapy for inoperable PGL. For patient with inoperable PGL, the medical therapy that can be offered is adequate blood pressure control and symptomatic treatment.

Poster

SUPERIOR VENA CAVA ONSTRUCTION (SVCO)–A PATIENT WITH REFRACTORY NON-HODGKIN LYMPHOMA

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We reported a case of an 80 years old man, with no comorbid presented with left neck swelling for two weeks with B symptoms. Clinically there is an enlarged left cervical lymph node size 8cm x 6cm with small dilated vein at the chest wall. A diagnosis of B-cell non-Hodgkin lymphoma was made from trucut biopsy of lymph nodes and stage IIIS,B based on findings in contrast enhanced computed tomography (CECT) of the neck, thorax, abdomen and pelvis. His disease also complicated with left internal jugular vein, subclavian vein and proximal brachiocephalic vein thrombosis and require subcutaneous Enoxaparin. First line chemotherapy Rituximab-Cyclophosphamide, Hydroxydaunorubicin, Oncovin and Prednisone (R-CHOP) was unable to administer due to recurrent infections. He was subsequently under palliative care. During his follow-up, he developed recurrent symptomatic superior vena cava obstruction (SVCO) and option of endovascular stenting was discussed with patient but not agreeable. He was then prescribed with short courses of Dexamethasone for symptomatic relieve. He survived the recurrent SVCO for almost 15 months but succumbed to an aspiration pneumonia. In conclusion, presentation of SVCO is common in advanced malignancy and survival is approximately 6 months. A good palliation with rapid and effective symptomatic relieve is often required. The choices of treatment include SVC stenting, palliative radiotherapy and bypass surgery. In current practice, patients with tumour recurrence or refractory disease, not fit for chemotherapy or radiotherapy due to poor performance status, salvage SVC stenting provides good SVCO symptomatic relieved as compared with usage of glucocorticoids.

Poster

PREVALENCE OF ALLERGIC RHINITIS IN CHILDREN WITH OTITIS MEDIA WITH EFFUSION

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Introduction: Prevalence of allergic rhinitis (AR) in persistent otitis media with effusion (OME) children in different countries varies between 82% to 93%. The association between AR and OME has been a controversial issue.
Objective: To determine the prevalence of AR in children with persistent OME, to identify the risk factors of OME, to identify the most common allergens associated with AR, to determine the hearing threshold of children with OME.
Methods: One hundred and thirty children were recruited and given 2 visits. During 1st visit history taking, physical examination and hearing assessment were done. Children with AR underwent skin prick test (SPT) and treated with intranasal steroid and antihistamine. After 3 months, children were re-examined and hearing assessment were repeated.
Results: Prevalence of AR in persistent OME children is 80.3%. Children with persistent OME are significantly more likely to have AR and larger household. The most common allergen that affect children with AR is house dust mites (87.7%). Otitis media with effusion caused a hearing loss up to 33dB. There was statistically significant improvement of the hearing threshold in visit 2. Hearing threshold in AR group is significantly impaired compared to non-AR group.
Conclusion: There is high prevalence rate of AR in persistent OME children. AR and extended family members are the significant risk factors for persistent OME. AR with OME had significant hearing loss compared to non-AR children with OME. There was marked improvement in the hearing threshold with medical therapy in OME children with AR.

Poster

THE VALUE OF PET-CT SCAN IN DETERMINING REMISSION STATUS IN LYMPHOMA PATIENTS INVOLVING THE HEAD & NECK REGION.

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Introduction: In lymphoma, Positron Emission Tomography-Computerized Tomography (PET-CT) generally provides greater prognostic information than conventional imaging. However, false positivitives can occur particularly in the head & neck, where lymphoid tissues have predilection for infection and inflammation.
Objective: To determine the association between positive scans in the head & neck at post-therapy with histology, and its diagnostic and prognostic values.
Methods: 488 PET-CT were retrospectively assessed between 2012-2016 (40 months). Positive uptakes in the head & neck (Deauville score 4) were biopsied.
Results: Prevalence of positive scans was 10.9% (53/488). Only two positive scans were histologically lymphomatous with mean maximum standardized uptake value (SUVmax) 9.0±2.69. False positives (96.2%) were histologically attributed to reactive lymphoid hyperplasia (SUVmax 9.0±3.88). Positive and negative predictive values, sensitivity and specificity were 3.8%, 100%, 100% and 89.5% respectively. False positives were associated with age, gender, extranodal involvement, Eastern Cooperative Oncology Group score (ECOG) score, positivity at the head & neck only and its pattern of positivity, although no significant predictors were identified. Hodgkin Disease (HD) was more likely to have positive scans at the head & neck only compared to Non-Hodgkin Lymphoma (NHL) (p=0.019). 106 patients with negative scans remained negative during study period, hence regarded as true negatives.

Conclusion: PET-CT scans ofthe head & neck post-therapy yielded high rates of false positives and should not be routinely performed. HD has higher likelihood of scan positivity at the head & neck than NHL. The value of PET-CT to detect true lymphomatous relapse in selected high-risk patients remains to be confirmed in future large clinical trials.

Poster

SYSTEMATIC REVIEW OF STATURE ESTIMATION IN SOUTH-EAST ASIAN POPULATION

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Background: Specific regression equation should be developed to determine stature for each population group as stature formulae are population-specific. Thus, this systematic review evaluates the availability of regression equations for stature prediction in the South-East Asia region.
Methods: In this systematic review, a search was done from SCOPUS database from January 2018 till March 2018, and Google Scholar was screened for research studies. The articles included were development in research studies of stature estimation in different populations, types of bones and the different methods used with different types of statures to generate regression equations.
Results: Seven studies were identified. These studies utilised methods such as radiographic images, direct bone measurement and body surface palpation and were able to yield regression equations by using different parts of bone.
Conclusion: This study revealed that linear regression analysis played an important role to estimate stature in different populations. It could be used as a guide for forensic anthropologists for stature prediction for both legal and humanitarian reasons.

Keywords: Systematic review, stature, regression equations, anthropology, forensic.

Poster

DEVELOPMENT OF A SEMICONDUCTOR SEQUENCING-BASED PANEL FOR SCREENING INDIVIDUALS WITH LYNCH SYNDROME

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Introduction: Lynch syndrome (LS) is associated with mutations in mismatch repair (MMR) genes and individuals who have one of these mutations have 20 to 65 % lifetime risk of colorectal cancer (CRC). Because inheritance of these mutations is autosomal dominant, close biological relatives are also at high risk. Early detection of CRC may lead to both better health outcomes and considerable savings in treatment costs.
Objective: To develop a rapid and sensitive method of screening LS.
Method: We designed an Ion Ampliseq™ Custom Panel with four MMR genes associated with LS (MLH1, MLH2, MSH6 and PSM2) and two genes which are not categorized as MMR genes (EPCAM and BRAF), for sequencing on the Ion Torrent PGM™ sequencer. Sequencing was performed on 16 DNA samples representing various stages of CRC. The sensitivity for mutation detection was determined by sequencing serially diluted DNA from two human cancer cell lines.
Results: We successfully identified variants that may associated with LS and validated in 19 samples using MassARRAY and Sanger sequencing. A pathogenic variant in MSH2 gene was identified in a 44 years old Dukes' D CRC patient. The Ion Torrent PGM clearly identified a single base pair C to T substitution in MSH2 gene with a variant frequency of 52%.
Conclusions: We achieved 92% specificity, 93.4% accuracy and a sensitivity of about 13% allelic frequency for the Lynch syndrome panel. With the development of this method, hereditary CRC can be detected at early stage using this rapid and sensitive approach.

Poster

EVALUATION OF THE POTENTIAL OF TOCOTRIENOL FROM *Bixa orellana* ON METABOLIC SYNDROME AND BONE LOSS IN A RAT MODEL

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Introduction: The underlying chronic inflammation and hormonal changes caused by metabolic syndrome (MetS) can result in osteoporosis. The beneficial effects of tocotrienol (a member of vitamin E family) on individual components of MetS and bone loss have been well-established.
Objective: This study aimed to evaluate the effects of tocotrienol derived from *Bixa orellana* (annatto seed) in preventing bone loss attributed to MetS in rats.
Methods: Age-matched twelve-week-old male Wistar rats were randomly divided into five groups (n=6/group). The baseline group was sacrifice upon received. The normal group was fed with standard rat chow. The remaining three groups were fed with high-carbohydrate high-fat (HCHF) diet to induce MetS. The diet regimen was assigned for 20 weeks. Starting from week 8, the HCHF animals were given tocopherol-stripped corn oil (vehicle), 60 mg/kg or 100 mg/kg annatto tocotrienol. At the end of the study, MetS parameters were evaluated before sacrifice. After that, the rats were euthanized. Blood and femurs were harvested for the evaluation of bone remodelling activity, microstructure, biomechanical strength, inflammatory markers, and hormonal levels.
Results: Supplementation of annatto tocotrienol improved all MetS parameters (except abdominal obesity), osteoblast surface, trabecular bone microstructure, bone strength ($p<0.05$). It also normalized the hormonal changes and inflammatory response in the HCHF animals compared to the vehicle-treated HCHF animals ($p<0.05$).
Conclusion: Annatto tocotrienol is a potential agent that can be developed to manage both MetS and osteoporosis concurrently. This may be achieved by supressing inflammatory response and hormonal changes caused by MetS.

Poster

RANDOMIZED CONTROL TRIAL SINGLE BLINDED STUDY OF *SILENCE* THROAT SPRAY IN THE TREATMENT OF SNORING – A PRELIM RESULT

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Introduction: Snoring is a low frequency sound produced by vibration of the upper airway walls during partial upper airway obstructions during sleep. *Silence* throat spray was introduced as one of the medical device that can improve symptoms of snoring.
Objective: To determine the effectiveness of *Silence* throat spray in reducing snoring.
Methods: A randomized control trial of *Silence* throat spray and placebo. They were assessed using Snore Outcome Survey (SOS) questionnaire and snoring visual analogue scale (VAS) to determine snoring intensity pre- and post treatment. The preliminary results were analysed for effectiveness of the treatment.
Results: A total 33 patients were enrolled in this study with a female to male ratio of 1.2:1 and mean age of 40.7. Majority of the patients (69.7%) were obese class I (BMI 27.6 – 34.9). Among all of the patients, 37.5% are primary snorer, 34.4% have mild OSA and 28.1% have moderate OSA with mean AHI of 10.9. There is significant improvement of snoring VAS using *Silence* throat spray, mean of 6.1 to 4.5 ($p = 0.006$) in compare with placebo. However, no significant difference was observed in SOS questionnaire.
Conclusion: *Silence* throat spray is an alternative to reduce snoring in primary snorer and OSA patient.

Poster

A PILOT GENOME WIDE ASSOCIATION STUDY ON PRIMARY ALDOSTERONISM IN MULTIEHNIC POPULATION OF MALAYSIA

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Introduction: Primary aldosteronism (PA) occurs due to the presence of aldosterone-producing lesions commonly located in the adrenal gland which can thus be cured by an adrenalectomy. Studies on surgically removed tissues found somatic mutations in five genes (*KCNJ5*, *ATP1A1*, *ATP2B3*, *CACNA1D*, and *CTNNB1*) can cause the excess aldosterone production. Most of these studies were performed in Caucasian patients.

Objectives: The aim of our study is to understand the genetic background which may promote somatic mutation in these genes and to investigate the frequency and distribution of these mutations in the multiethnic Asian population in Malaysia.

Methods: To characterize the genetic background of PA, a pilot genome wide association study (GWAS) was performed using the Human Infinium OmniExpressExome-8 v1.4 BeadChip to compare gDNA of PA patients (N=47) with healthy controls (N=33). The Association Workflow in Partek® Genomics Suite™ was used and association analysis was performed using the Chi-square Test and reported as an odds ratio (OR). On tumour DNA, targeted sequencing of hotspots for the five causal genes were performed on 54 aldosterone-producing adenomas (APAs) patients.

Results: From the pilot GWAS analysis, 69 SNPs with p-value less than $5x10^{-8}$ were identified to be associated with PA but only one SNP is within a gene, *EPHA4*. Interestingly *EPHA4* is known to bind to *Efnb3* which when knockedout in mice, causes enhanced constriction in the carotid arteries (Wang et al., 2016). As for prevalence of somatic mutations, the most prevalent is the *KCNJ5* mutation (31.5% of APAs). The highest number observed in Chinese patients (33.3%), followed by Malay patients (30.8%).

Conclusion: To note, unlike previous findings in Caucasian cohorts, *KCNJ5* mutation were present more in males Chinese (39.3%) with an average age of 50±11 years old and germline mutation in *EPHA4* gene were associated with PA.

32nd Scientific Meeting Malaysian Society Pharmacology & Physiology (MSPP) 2018

"*Translating Medical Science into Sustainable Health Care*"

8-9 August 2018

Hotel Bangi Putrajaya

Plenary Lecture

ROLE OF NUTRITION IN TACKLING MAJOR HEALTH ISSUES IN MALAYSIA

TRANSLATING MEDICAL SCIENCE INTO SUSTAINABLE HEALTH CARE

PROFESSOR EMIRITUS DATO' DR. KHALID BIN TAN SRI ABDUL KADIR

Monash University

Research in the basic medical sciences has improved with the availability of new technologies and ability to utilize new molecular and genetic manipulations resulting in new understanding of basic physiological and pharmacological of metabolic processes and diseases. The ultimate aim is to be able to diagnose diseases and metabolic derangements early and accurately, and come up with new treatment modalities, or cure or preventive measures. Although only a small percentage of basic medical research eventually result in new cures or products, the impact of recent discoveries has greatly transformed our ability to prolong life in previously incurable diseases or cancers, and improved the health of whole populations e.g. by vaccination against old and new diseases. The main issues are the escalating costs of doing research, especially basic scientific research which has no immediate clinical benefit, and the high cost of the eventual products entering the markets. Research however is the basis of progress, even in developing countries which can ill afford it unless it can be translated into improving health care.

Plenary Lecture

ROLE OF NUTRITION IN TACKLING MAJOR HEALTH ISSUES IN MALAYSIA

SUZANA SHAHAR

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Non-communicable diseases have been identified as major cause of morbidity and deaths in Malaysia, predominantly due to unhealthy urban lifestyle (e.g. work stress, being sedentary and unhealthy eating habits). Malaysia is also experiencing aging phenomenon. The 2016 World Health Assembly multi sectorial action for a life course approach to healthy aging stated that "most of the health problems of older age are linked to chronic non-communicable diseases which can be prevented or delayed by healthy behaviours," and among the most important of these is a healthy diet. Further, dietary risks have been identified as the leading risk factor for disease and disability in the country. Tackling major health issues through prudent diet and nutrition perspectives require multidimensional and multi sectorial approaches, from individual behaviours, environment and community support, structured programmes and policies. In particular, nutrition component should be integrated in all aspects of health promotion and strategies for future developments including cities for all ages, smart cities and green space and technology. In conclusion, food is a basic and thus essential needs of individuals to survive. A wholesome nutrition is a key element for healthy lifestyle and longevity that reduces the risk of NCD and its undesirable impact on health and social burden of the nation.

Plenary Lecture

APPLICATION OF OMICS-BASED MEDICINE IN TODAY'S ERA

NORFILZA MOHD MOKHTAR

Universiti Kebangsaan Malaysia

The traditional approach to study a disease has concentrated on a single event, for instance a single gene mutation or function. With the completion of Human Genome Project, there has been significant advancement of new range of tools in science that permits the holistic view on how genes could alter the homeostasis of signalling networks within cells and gene-gene interaction with cells that link with the local environment. The high-throughput omics technologies have enabled the comprehensive number of measurements over short of time giving in-depth information on individual's DNA, RNA and protein. The integration of these data permits accurate modelling of complex disease network. However, our skills to interpret the molecular mechanism that regulate complex relationship remain limited. Biological mechanisms are complex and this coupled with the noisy nature of experimental data such as cellular heterogeneity as well as sampling issues, contaminated from neighbouring tissues may seriously affect the data. Another challenge is the bioinformatics analysis of the data that may lead to the wrong interpretation. It becomes more obvious that the bottleneck in the laboratories has moved from data generation to data management and interpretation. Precision medicine is the way in near future. Scientists have to prepare for the benefit of future approach to treatment. The cross border collaborations between clinicians, pathologists, scientists and bioinformatician are highly encouraged in trying to match the treatment with the disease characteristics using the information from the holistic approaches.

Plenary Lecture

EFFECT OF VASCULAR AGING ON THE HEART AND BRAIN

ALBERTO AVOLIO

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The pressure pulse generated by ventricular ejection travels throughout the arterial vasculature at a velocity determined by the stiffness of large arteries. With ageing large arteries increase in stiffness with an associated increase in pulse wave velocity. This contributes to the increase in pulse pressure with age, increasing ventricular load.

The pulse amplitude of blood flow scales to vessel calibre and decreases with distance from the heart; however the amplitude of the corresponding pressure pulse is determined by arterial stiffness and wave propagation phenomena and generally increases with travel towards the periphery. In youth, the central aorta is relatively more distensible than peripheral arteries, presenting a low impedance, thus buffering pulsatile energy. With increasing age there is reduced buffering of central aortic pulsatility due to increased aortic impedance. The system becomes more uniformly stiff, thus enabling pulsatile energy to reach further into microcirculatory beds, affecting end organs.

The pulsatility of pressure and flow in the cerebral vasculature can influence perfusion pressure through interaction with intracranial pressure as well as causing potential damage to the microcirculation. Increased mechanical stress on cerebral endothelial cells can also affect the mechanotransduction and cell signalling pathways resulting in modulation of protein expression. Experimental evidence will be presented that suggests that cyclic mechanical stretch on cerebral endothelial cells can potentiate expression of the amyloid precursor protein, thus establishing a possible link between large artery function, vascular stiffness, pulse pressure and potential vascular causes of cognitive impairment and dementia, leading to Alzheimer's disease.

Plenary Lecture

PERIVASCULAR ADIPOSE TISSUE, AMPK AND THE MODULATION OF VASCULAR FUNCTION

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Perivascular adipose tissue (PVAT) positively regulates vascular function by releasing factors such as adiponectin. The enzyme AMP-activated protein kinase (AMPK) is present in PVAT and may mediate the vascular effects of adiponectin. Here we used mice deficient in AMPK 1 as well as an obesogenic high fat diet (HFD) to study regulation of vascular function by PVAT under normal and hyperlipidaemic conditions.

Wild-type (Sv129) or 1AMPK knockout (KO) mice were fed either normal diet (ND) or HFD (42% kcal fat) for 12 weeks. Vascular function was studied in denuded aortic rings either with or without PVAT and adiponectin release by PVAT measured using ELISA. Immunohistochemistry and real-time qPCR was used to detect macrophages in PVAT and immunoblotting used to measure expression of AMPK following HFD. PVAT augmented relaxation to cromakalim in WT but not KO mice via release of a transmissible factor. KO PVAT secreted significantly less adiponectin. Globular adiponectin augmented relaxation in both WT and KO aortic rings while an adiponectin blocking peptide significantly attenuated relaxation in WT rings with PVAT but not KO rings. In WT mice, HFD increased infiltration of macrophages, reduced adiponectin secretion and attenuated the anticontractile effect; accompanied by reduced AMPK phosphorylation. In KO mice, PVAT was already dysfunctional and HFD had no effect. AMPK 1 has a critical role in maintaining the anticontractile actions of PVAT; likely via altered adiponectin secretion or sensitivity. High-fat diet mimics many of the effects of AMPK knockout, suggesting that AMPK may protect the vessel against deleterious changes in response to HFD.

Plenary Lecture

METABOLIC SYNDROME, OSTEOPOROSIS AND PALM VITAMIN E

IMA NIRWANA SOELAIMAN[1], WONG SOK KUAN[1], FAIRUS AHMAD[2], CHIN KOK YONG[1]

[1]Department of Pharmacology and [2]Department of Anatomy, Faculty of Medicine, Universiti Kebangsaan Malaysia.

Chronic inflammation caused by metabolic syndrome (MetS) can result in osteoporosis. The beneficial effects of tocotrienol, a subtype of vitamin E, on individual components of MetS are well documented. Our earlier research has also proven that tocotrienol can prevent and reverse bone loss in osteoporosis due to various causes. However, the effects of tocotrienol treatment on all the components of metabolic syndrome, simultaneously with the effects on bone loss, has not been studied. Palm oil derived vitamin E contains 78.1% tocotrienol isomers and 21.9% -tocopherol. This study aimed to determine the effects of palm vitamin E mixture on the conditions associated with metabolic syndrome, as well as on the subsequent bone loss due to the syndrome. MetS was induced by feeding three-month-old male Sprague-Dawley rats with high-fat high-carbohydrate (HCHF) diet for 20 weeks. Starting week 8, the rats were randomized into three groups and given either palm vitamin E mixture at 60 mg/kg or 100 mg/kg, or vehicle. Metabolic syndrome parameters and bone microstructural changes were examined at regular intervals. The bones were harvested for biomechanical strength test after the rats were sacrificed at week 20. We found that supplementation of palm vitamin E mixture (60 or 100 mg/kg) prevented hyperglycaemia, hypertension, and dyslipidaemia and also improved trabecular bone microstructure and strength in rats fed with HCHF diet. Besides, palm vitamin E significantly reduced IL-1 and IL-6 level, as well as leptin level in rats fed with HCHF diet ($p<0.05$). In summary, palm vitamin E is a potential agent that can be developed to treat both MetS and osteoporosis concurrently.

Symposium

GUT MICROBIOME AT THE FRONTIER OF PRECISION MEDICINE

RAJA AFFENDI RAJA ALI

Universiti Kebangsaan Malaysia

In the past decade, the role of the gut microbiome in human health and diseases have been one of the most evolving fields in medical research. Precision medicine implies an emerging approach for disease treatment and prevention that takes into account patient variability in genes, environment and lifestyle and this certainly include gut microbiome. The contribution of gut microbiome to human diseases as well as the potential utilization of the microbial modulation in the prevention and treatment of certain human diseases, in particular for the gastrointestinal disorders are well established. Diagnosing, managing and monitoring many human diseases required many targets and patient-specific target such as gut microbiome which has great potential (targeting and manipulating in the context of specific disease) in the era of precision medicine. The current method of choice for analysing gut microbiota composition is using next-generation sequencing. In this presentation, I will summarize the established and the postulated correlations between gut microbiome and disease pathogenesis in the fields of gastroenterology and highlighting the specific microorganisms that have been identified as potential therapeutic targets.

Symposium

FUSION MEDICINE: MANAGING HYPERTENSION IN LOW RESOURCES SETTINGS

AINI HAMID

University of Nottingham

Focusing on Vietnam's rampant prevalence in hypertension (HPT) and increasing burden from non-communicable diseases (NCDs), this study explores the use and questions the effectiveness of traditional medicine (TM) combined with modern medicine (MM) practices as a sustainable approach in low-income healthcare settings.

A literature search indicates HPT is primarily managed in Vietnam using MM but there is a large dependency on WHO funding. There is scarce information on how HPT is managed once the funds ran out. A week long exploratory visit to hospitals and clinics in Hanoi city and surrounding districts took place and included face-to-face interviews with healthcare professionals and Directors of Hospitals. Our exploration confirmed the large extent of dependency on WHO funded NCD programmes. The visit also revealed the equally large dependency of the healthcare system on fusion medicine (FM). MM practitioners were highly receptive towards TM, their acceptance may stem from their unique medical degree curricula. Our visits to the local "communes" or rural health facilities revealed that within the vicinity of a modern clinic or hospital lays herb gardens where patients are educated on identification, methods of preparation and the mode of administration of TM herbs to better manage the disease alongside their MM drugs.

The availability of these plants that costs near to nothing is key for the low-income population. FM is widely accepted and popular in Vietnam and if its effectiveness is eventually scientifically proven, the FM model could be adopted for a more sustainable healthcare system regardless of economic status.

Symposium

STANDARDIZATION OF OOCYTE QUALITY TO ASSESS SPERMATOZOA FERTILIZATION CAPABILITY IN ANIMAL MODEL

SITI FATIMAH IBRAHIM

Universiti Kebangsaan Malaysia

Sperm assessment has always been centred towards its ability to fertilize an oocyte. Despite a simple concept, spermatozoa fertilization capability has also been assumed using various indirect methods. Most common methods are sperm viability through sperm count, sperm movement (CASA), capacitation status (Hoest), DNA integrity (Comet assay) and sperm morphology (droplets and overall structure). Despite numerous papers associating these factors to spermatozoa fertilization capability, reproducibility of successful percentage between research labs have been low. Hence, direct sperm fertilization capability should be conducted to produce a much more reliable and reproducible end result. Despite a simple solution, a major hurdle to this issue is the inability to obtain standard matured oocytes. Short of developing cloned oocytes, this talk will discuss various factors that our lab found is essential to produce a near similar quality of oocytes. As a teaser, factors that were found to be essential were apoptosis expression - cleavage rate, cumulus cell characteristics classification, and the annexin-V factor.

Symposium

BIOMAKER IN ALZHEIMER DISEASE: CURRENT STATE OF TRANSLATIONAL RESEARCH

WAEL MOHAMED

International Islamic University Malaysia

Alzheimer's disease (AD) is a brain disorder associated with slow, progressive loss of brain function mostly in older people. It is irreversible and relentless with death occurs between 4-8 years. The proportion of the total population who were elderly had increased steadily from 4.6% in 1957 to 5.7% in 1990. It is also predicted that the proportion will continue to increase from 6.3-7% in the 2000s to 12-14% by the year 2030; hence, our urgent need for early diagnosis of the disease as well as the clinical assessment of disease progression. There are no cures or disease-modifying therapies, and this may be due to our inability to detect the disease before it has progressed to produce evident memory loss and functional decline. In principle, it may be possible to advance the diagnosis much earlier by improving the predictive validity of the prodromal risk indicators based upon cognitive decline and subjective impairment. One widely advocated approach is the incorporation of disease biomarkers that may indirectly represent the extent of underlying neuropathology.

Symposium

EMERGING ROLE OF MICROTHROMBOSIS IN THE MANIFESTATIONS OF THE CEREBRAL SMALL VESSEL DISEASE (CSVD) SPECTRUM

MUZAIMI MUSTAPHA

Universiti Sains Malaysia

The term cerebral small vessel disease (CSVD) refers to a heterogeneous group of pathological processes with numerous aetiologies affecting small, microcirculation of the brain. On magnetic resonance imaging (MRI), CSVD correlates include lacunes, subcortical infarcts, white matter hyperintensities, enlarged perivascular spaces, microbleeds, and brain atrophy – manifesting as symptomatic stroke, or as asymptomatic/silent stroke (the latter being commoner). The ischaemia of the small vessels is thought to arise from structural restrictions of the vessel lumen and membrane wall, or for its functional dysregulation, leading to a state of chronic hypoperfusion that is responsible for incomplete infarct or acute focal necrosis or called as lacunar infarct. Intriguingly, such an infarct in the deep white matter is often found as an incidental MRI finding, or termed 'silent brain infarcts'. An emerging, and largely unexplored thrombogenic player to this ischaemic CSVD aetiology is the vascular endothelial microparticles. This review aims to summarize the current knowledge about microartheroma and microthrombosis of small arteries in the brain, and postulate their plausible roles in CSVD manifestation.

Symposium

MANAGEMENT OF EPILEPSY IN THE 21ST CENTURY

RAYMOND AZMAN ALI

Universiti Kebangsaan Malaysia

Epilepsy is the 3rd commonest chronic neurological problem seen in the neurology outpatient clinic. Monogenic epilepsy accounts for only 2% of all epilepsies. However, knowing the gene responsible for epilepsy will avoid unnecessary diagnostic tests, facilitates family planning, enhances the discovery of new mutations and assists the selection of effective therapy. It is known that different patients respond and react differently to different antiseizure drugs (ASD). Genetic factors contribute significantly to this variability. Precision medicine (PM) is a relatively new medical model that customizes healthcare using molecular analysis. PM is aimed at maximising drug efficacy and reducing adverse events, which may be lethal. Molecular research in epilepsy has focussed on identifying such susceptibility genes, resistance genes (genes conferring resistance to ASD), pharmacogenomics and genes predicting adverse drug reactions. Association of the drug transporter gene ABCB1 with resistance to certain antiseizure drugs, unfortunately also, has not been replicated in several studies, including ours. Recent evidence supports the association of the HLA-B*1502 allele (which is common among in Southeast Asia) and other alleles with severe cutaneous adverse reactions to carbamazepine, and possibly also lamotrigine and phenytoin. More recently, the HLA-B*3801 allele has been shown to be associated with lamotrigine-induced SJS/TEN. There has been controversy surrounding the cost-effectiveness of HLA screening. We at UKMMC are in the midst of commercialising a fully portable rapid test kit to save both time and costs. With better understanding of the biologic consequences of these gene mutations and polymorphisms, we may in the near future, be able to design better drugs and individualise therapy for epilepsy.

Symposium

INVOLVEMENT OF SPHINGOSINE KINASE 1 IN PHASE 1 OF THE HYPOTENSIVE REPONSE TO ANANDAMIDE IN THE ANAESTHETISED MOUSE

SIMON KENNEDY

University of Glasgow, UK

In the isolated rat carotid artery, the endocannabinoid anandamide (AEA) induces endothelium-dependent relaxation via activation of the enzyme sphingosine kinase (SK). This generates sphingosine-1-phosphate (S1P) which can be released from the cell and activates S1P receptors on the endothelium. In anaesthetised mice, AEA has a well-characterised triphasic effect on blood pressure but the contribution of SK and S1P receptors in mediating changes in blood pressure has never been studied. Therefore, we assessed this in the current study. The peak hypotensive response to 1 and 10 mg/kg AEA was measured in control C57BL/6 mice and in mice pretreated with selective inhibitors of SK1 (BML-258, also known as SK1-I) or SK2 ((R)-FTY720 methylether (ROMe), a dual SK1/2 inhibitor (SKi) or an S1P1 receptor antagonist (W146). Vasodilator responses to S1P were also studied in isolated mouse aortic rings using myography. The hypotensive response to AEA was significantly attenuated by BML-258 but not by ROMe. Antagonising S1P1 receptors with W146 completely blocked the fall in systolic but not diastolic blood pressure in response to AEA. In pre-contracted endothelium-intact aortic rings, neither S1P nor AEA induced significant relaxation despite expression of S1P1 receptors throughout the vessel wall. The rapid phase 1 hypotensive response to AEA in vivo requires the SK1/S1P regulatory-axis. The mechanism may be via an S1P1-mediated fall in total peripheral resistance but this does not occur within conduit vessels. These findings have important implications in our understanding of the hypotensive and cardiovascular actions of cannabinoids.

Symposium

CARDIOVASCULAR DISEASE RESEARCH IN MALAYSIA: CHALLENGES AND OPPORTUNITIES

OTEH MASKON

Universiti Kebangsaan Malaysia

Cardiovascular disease is one of the practices that rapidly evolves especially in pharmacotherapy and intervention. Malaysia has been involved in many of the multicentre clinical trials the result of which have contributed to advancement in the treatment of CV diseases, such as acute coronary syndrome/IHD and heart failure (HF). There are also opportunities to lead in the research or expertise in the Asian/ Asian Pacific region at least, taking the case of treatment options for patients with end-stage HF. Japan and Korea have been the leaders in this area, however there are potentials for Malaysia to come forward in the cardiac regenerative therapy for patients with end-stage HF. Japan has initiated a new method of cell sheet therapy based on myoblast, and soon moving on to induced pluripotent stem cells (iPS). Malaysia has the expertise in cell therapy and GMP lab capable of harvesting mesenchymal stem cells. Due to issues with importing the Japanese technology, we have been assured that our own expertise is able to produce our own MSC cell sheets. There are several challenges ahead, the biggest which is funding, since research in regenerative medicine typically cost multimillion ringgits. From past experience, a single centre based research in regenerative medicine can be met with many limitations in term of budget, patient recruitment as well as manpower. As a conclusion we are presenting a new paradigm in cardiac regenerative therapy using myocardial cell sheets concept based on mesenchymal stem cells, which can be harvested locally. Learning from past experience, the way forward in this initiative has to come in a multicenter, national collaborative efforts. Since substantial funding would be required, we propose to start with a 'pilot' study involving a small number of patients, requiring a smaller funds while attempting to prove the viability of this high impact project.

Symposium

BIOMAKERS OF VASCULAR FUNCTION: NON-INVASIVE ASSESSMENT AND CLINICAL APPLICATION

ALBERTO AVOLIO

University of Macquarie, Australia

The function of blood vessels is to distribute blood throughout the circulatory system driven by pulsatile ventricular ejection. Arteries act as conduits for the moving blood and the properties of the wall do not allow them to collapse at low pressure. Veins are capacitive vessels that contain the major part of the blood volume, they are thin-walled and function as collapsible tubes. This presentation will focus only on arterial function, with arteries as distensible blood conduits, endothelial function and arterial stiffness associated with arterial pressure. Noninvasive measurements of arterial function have been conventionally done to assess obstructive phenomena such as atherosclerotic plaques, factors that limit blood flow. These include imaging modalities, with the most common in routine clinical use being ultrasound, where arterial structure can be quantified as wells as flow parameters (eg pulsatility index). Arterial stiffness is measured indirectly by pulse wave velocity. Since it is dependent on blood pressure, techniques have been developed to obtain measures of pressure-independent arterial stiffness, as better biomarkers of intrinsic changes in arterial wall properties. Arterial models have enabled the estimation of central aortic pressure from the peripheral pulse as an improved biomarker of ventricular load. Features of the central and peripheral pulse are also examined for vascular information. Nonivasive quantification of the hyperaemic response to vascular occlusion have enabled measurement of endothelial function for assessment of flow-dependent phenomena in vascular reactivity. These biomarkers will be discussed in relation to their respective potential for clinal assessment of arterial function.

Symposium

MULTIPLE MEDICAL BENEFITS OF EDIBLE BIRD'S NEST EXTRACTS

CHUA KIEN HUI

Universiti Kebangsaan Malaysia

Edible bird's nest (EBN) is a renewable product that made from swiftlet's (*Aerodramus fucifagus*) special glands secretion during breeding season. Although EBN has been taken by Chinese for its nutri-pharmaceuticals benefits since few hundred years ago, it has not been popular in other races. Besides the price issue, the medical and scientific evident of EBN effects is only actively investigated for the past 15 years. The active compounds in the EBN which contributed to the medical benefits were identified as glycoprotein or glycopetides. EBN glycopeptide is water soluble and can be extracted by using hot water and enzymatic digestion. The very well-known EBN effect on skin rejuvenation was demonstrated using human dermal fibroblasts isolated from skin. The EBN extract added into the fibroblasts culture promoted its proliferation, increased the wound healing rate and increased the anabolic synthesis of skin extracellular matrix like collagen and elastin. At the same time, EBN extract reduced matrix metalloproteinase 1 (MMP1) production. One of the controversial issues of taking EBN for health is in cancer patient. Through a proprietary extraction method, the extracted EBN showed anti-cancer properties against MCF7, a breast cancer cell. It triggered apoptosis in cancer cells mainly by intrinsic pathway. When EBN extract was applied together with tamoxifen, the cancer killing effect was enhanced. This synergistic work between EBN and tamoxifen could bring a new strategy of cancer therapy in the future.

Symposium

NEW PHARMACOLOGICAL APPROACH OF NATURAL PRODUCT RESEARCH FOR DISCOVERY OF NEW DRUG LEADS

IBRAHIM JANTAN

Taylor's University

The single target approach has been the dominant paradigm to discover natural small molecules as new leads for the development and discovery of drug targets. However, the reductionist approach had generally declined due to the many major hurdles faced, such as difficulties in obtaining sufficient supply of high quality natural products libraries, ownership issues and research in this field is lengthy, expensive, highly complex and ineffective with low success rate. Natural products drug discovery has been marginalized in favour of the rational design of synthetic compounds to target specific molecules after the advent of high throughput screening (HTS), combinatorial chemistry and advancement in the knowledge of molecular mechanisms, cell biology and genomics. However, there is a recent revival of interest in natural products research due to the emergence of new technologies in spectrometry and spectroscopic techniques, advances in screening methodologies, development of molecular biology and biotechnology and use of computer technology in rational drug design. Recently there is a growing interest to use innovative approaches to drug discovery from natural products by network pharmacology. The integrated multidisciplinary concept of multiple targets, multiple effects and complex diseases in network pharmacology have enriched our understanding of complicated pathogenesis and multi-target pathologies of systemic diseases and reduced difficulty in identifying relevant interventions to target such complexities. The omics technologies in system biology have now been widely used to correlate and elucidate multiple targets and network of human diseases and drug actions. Herbal medicines may serve as valuable resources for network-based multi-target drug discovery.

Symposium

DRUG NANODELIVERY SYSTEM IN RESOLVING POOR BIOAVAILABILITY OF POLYPHENOLS

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The development of drug nanodelivery system allows with the delivery of chemical substance to the specific disease tissue without harming the healthy tissue. Besides, the utilisation of this technology increases the bioavailability of polyphenols at the disease site, which increases its bioefficiency In addition, this technology has also been used as a strategy to reduce toxicity and side effects associated with particular drugs.Polyphenols have received enormous attention in pharmaceutical research and development due to their potential health benefits (e.g., antiaging, antioxidant, anti-inflammatory, cholesterol-lowering or anticancer) despite the uncertainties about their bioavailability. Polyphenols have been reported to exert favourable pharmacological activities especially in in vitro and in vivo models. However, the effect seen in vitro is not clearly translated into in vivo models. One of the major reasons are inconsistent and low systemic exposure or poor oral bioavailability of polyphenols greatly limits its therapeutic uses. We have utilised inorganic layered hydroxide as a host to construct organic-inorganic nanoparticles to deliver polyphenols. The synthesised nanoparticles were characterised to determine their physicochemical properties and various assays were conducted to determine its specificity and efficacy. Analysis was conducted to compare the activity of the developed nanoparticles compared to the respective pristine drug. Our observations have suggested that drug nanodelivery system may be an important strategy necessary to resolve the bioavailability issues faced by polyphenols.

EARLY LIFE INTERVENTIONS AND PRENATALLY PROGRAMMED HYPERTENSION

LEE SIEW KEAH

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Oxidative stress during critical growth and development periods, like during the intrauterine and immediate postnatal periods, has been proposed to contribute to increased incidence of hypertension in later life. Whether intervention during early foetal life or immediate postnatal life could modify the subsequent development of prenatally programmed hypertension is unclear. We hypothesized that (i) perinatal renal oxidant/antioxidant imbalance plays a role in prenatally programmed hypertension in spontaneously hypertensive rats (SHR), (ii) early exposure to melatonin, a potent antioxidant, is able to restore the defective oxidant/antioxidant system, and therefore prevent the rise in blood pressure in SHR, (iii) immediate change in postnatal maternal environment could prevent the development of hypertension in SHR. Our data confirmed that mis-programmed renal hydrogen peroxide detoxification mechanism (downregulated glutathione peroxidase and upregulated catalase level), occurred at early pre-hypertensive stage of SHR, and it could be the culprit in the pathogenesis of hypertension in adult SHR. To investigate if early intervention could prevent the rise in blood pressure, melatonin was given to SHR dams from as early as day 1 of pregnancy. Interestingly, the rise in blood pressure in the pups was delayed with increased level of renal glutathione peroxidase activity. We further hypothesized that the dysregulated renal oxidant/antioxidant system and development of hypertension in SHR could be corrected via modification of pre-weaning maternal environment. SHR pups reared by normotensive WKY dams had a better body weight gain, and delayed rise in blood pressure with reduced renal lipid peroxidation (thiobarbituric acid reactive substances) level. However, the hypotensive effect and reduction in oxidative stress associated with the change in maternal environment were short-lived and disappeared as blood pressure rose to levels of those in the controls, albeit slightly later. We further postulated that combination of perinatal melatonin supplementation and cross-fostering technique might be able to better ameliorate the development of hypertension in adult SHR. But it appears that the combination of cross-fostering and perinatal melatonin supplementation did not exert the expected synergistic effect on delaying or ameliorating the rise in blood pressure in SHR. In conclusion, our findings suggest that melatonin supplementation and changes in postnatal maternal environment might delay the rise in blood pressure in SHR but they do not prevent the development of hypertension in SHR.

'BONE HEALTH AMONG MALAYSIAN MEN AND THE POTENTIAL OF TOCOTRIENOL IN PREVENTING MALE OSTEOPOROSIS

KOK-YONG CHIN

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Male osteoporosis is a medical issue constantly neglected by the medical community and public alike. Despite having a lower prevalence, men suffer from greater morbidity and mortality compared to their female counterparts after a fragility fracture. However, most men are not aware of their bone health. To address this deficiency, a bone health screening was performed for men aged >20 years in Klang Valley between 2009-2011 using calcaneal quantitative ultrasonometry. Data pertaining to body anthropometry, lifestyles, vitamin D and hormone levels of the subjects were also collected. The results showed that approximately 24% of the participants had a moderate to high risk of osteoporosis. Age, age-related changes in hormone level, particularly sex hormone-binding globulin, free and bioavailable testosterone, physical activity, height and body mass index were significant predictors for bone health in men. Approximately 23% of the participants also suffered from vitamin D insufficiency defined by 25-hydroxyvitamin D level. However, vitamin D level was not associated significantly with bone health in these subjects. Therefore, bone health status in Malaysian men deserved more attention. The currently available prophylactic options for osteoporosis are limited to calcium and vitamin D. Tocotrienols, a group of vitamin E isomers, have been shown to prevent osteoporosis in animal model of oestrogen deficiency. Since bone loss in men is partially explained by the age-related decline in testosterone and the evidence regarding the efficacy of tocotrienol in preventing osteoporosis due to testosterone deficiency is limited, a series of studies assessing the efficacy of tocotrienol mixture derived from annatto bean in preventing bone loss in primary (orchidectomy) and secondary (drug-induced) androgen deprivation models was performed. Annatto tocotrienol (60-100 mg/kg/day) was administered to orchidectomized rats or rats receiving buserelin (gonadotropin-releasing hormone agonist) for 2-3 months. The results showed that annatto tocotrienol prevented microstructural deterioration of the rats suffering from androgen deficiency. The bones of the supplemented rats also endured a higher biomechanical stress and had a higher calcium content. Gene expression analysis in the supplemented rats showed higher expression of genes coding for alkaline phosphatase, collagen type I alpha 1, beta-catenin, osteopontin, and a lower expression of the gene coding for receptor activator of nuclear factor kappa-β ligand. It is hypothesized that the skeletal action of annatto

tocotrienol is predominantly anabolic because the genes upregulated are related to bone formation. As a conclusion, annatto tocotrienol could prevent bone loss in men caused by androgen deficiency through its skeletal anabolic action.

GLUTAMATE HYPEREXCITABILITY: ROLE OF PKC EPSILON IN ETHANOL WITHDRAWAL-INDUCED ANXIETY

JAYA KUMAR

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Myriad of studies have implicated metabotropic glutamate receptor 5 (mGlu5) and Protein Kinase C (PKC) epsilon in alcohol dependence. Antagonists against mGlu5 were shown useful in reducing binge ethanol intake, whereas genetic elimination of gene encoding PKC epsilon (PRKCE gene) also decreased alcohol consumption and severity of withdrawal symptoms. Further laboratory findings revealed mGlu5 to be functionally linked to PKC epsilon at drug addiction-related brain regions. In line with this progress, we have investigated the role of amygdalar mGlu5-PKC epsilon mediated signalling pathway in the manifestation of ethanol withdrawal (EW) induced-anxiety. We fed male Wistar rats with a modified liquid diet (MLD) containing low fat cow milk powder, maltodextrin, sucrose and ethanol for 20 days. On day 21, ethanol was withdrawn from the diet and the animals were exposed to open field and elevated plus maze to be assessed for abstinence-induced hyperanxious state. An hour prior to behavioural assessment, the rats were intraperitoneally administered with normal saline, mGlu5 antagonist (2.5, 5, 10, 20, 30 mg/kg), and acute ethanol (2.5 g/kg, v/v 20%), respectively. We reported a marked increase in protein and gene expression of mGlu5 and PKC epsilon in the amygdala during the hyperanxious state. There was also profound increase in the expression of phosphorylated (S729) PKC epsilon during the EW-induced anxiety. Administration of mGlu5 antagonist, MPEP (10 mg/kg) significantly attenuated the abstinent-induced glutamatergic hyperexcitability and hyperanxious state, seemingly via a PKC epsilon-mediated pathway in amygdala. Intriguingly, acute administration of ethanol attenuated withdrawal anxiety, however without affecting the amygdalar expression of phosphorylated PKC epsilon (S729) level, suggesting ethanol may not have a direct effect on PKC epsilon during EW-induced anxiety. As predicted, acute ethanol challenge significantly reduced the gene expression of mGlu5, reflecting the universal inhibitory effects of ethanol on glutamate receptors.

FPP001

THE PHARMACOKINETICS OF 18F-FLUOROCHOLINE IN BREAST CANCER PATIENTS

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Aims: Breast cancer can be due to abnormal choline (Cho) metabolism. Earlier studies indicated that Cho uptake is varied among the different subtypes of breast cancer. Apart from the ubiquitous 18F-Fluorodeoxyglucose (18F-FDG), the 18F-Fluorocholine (18F-FCH) also has been developed as an oncologic probe for PET/CT imaging modality. This study aims to evaluate the kinetics and radiation dosimetry of 18F-FCH using human biodistribution data.
Methods: The biodistribution of 18F-FCH was obtained at two different time points, i.e. 6 minutes and 30 minutes after administration 18F-FCH. The biodistribution data were collected within the first hour post-injection from the attenuation-correction of whole-body PET scans. The estimation of radiation dosimetry was then calculated using human biodistribution data assuming no redistribution of tracer after 1 h.
Results: The 18F-FCH clearance from the blood was foAims: Breast cancer can be due to abnormal choline (Cho) metabolism. Earlier studies indicated that Cho uptake is varied among the different subtypes of breast cancer. Apart from the ubiquitous 18F-Fluorodeoxyglucose (18F-FDG), the ^{18}F-Fluorocholine (18F-FCH) also has been developed as an oncologic probe for PET/CT imaging modality. This study aims to evaluate the kinetics and radiation dosimetry of 18F-FCH using human biodistribution data.
Results: The 18F-FCH clearance from the blood was found to be very rapid in humans with little changes in the biodistribution pattern seen after >5 minutes post-administration. Meanwhile, the 18F radioactivity concentration in the arterial blood reached a constant level >3 minutes after administration of 18F-FCH. The average standardized uptake value (SUV) of the liver was 10 times higher than in the tumours. Interestingly, there was a significant correlation between malignant and benign breast cancer, with the former showing high 18F-FCH uptake of 1.66$\pm$0.26 g/dl compared to the latter, which was 0.56$\pm$0.14g/dl.

Conclusion: The 18F-FCH is rapidly cleared from the blood circulation and its biodistribution changes very slowly at >5 minutes after administrationund to be very rapid in humans with little changes in the biodistribution pattern seen after >5 minutes post-administration. Meanwhile, the 18F radioactivity concentration in the arterial blood reached a constant level >3 minutes after administration of 18F-FCH. The average standardized uptake value (SUV) of the liver was 10 times higher than in the tumours. Interestingly, there was a significant correlation between malignant and benign breast cancer, with the former showing high 18F-FCH uptake of 1.66±0.26 g/dl compared to the latter, which was 0.56±0.14g/dl.

FPP002

MICRORNA-200c PROMOTES PROGRESSION AND METASTASIS BY SUPPRESSING DLC-1 IN SEROUS EPITHELIAL OVARIAN CANCER

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Aims: Serous epithelial ovarian cancer (SEOC) remains the most lethal gynaecological cancer with high metastatic properties leading to poor prognosis in advanced stages (stage III and IV). Our recent miRNA profiling discovered miR-200c to be significantly up-regulated by 8.92 fold compared to normal ovarian tissues. The aim of this study was to investigate the roles of miR-200c in regulating its targeted gene, DLC-1 expression in SEOC tissues and metastatic SKOV3 cell line.
Methods: Fresh frozen tissues of normal and ovarian cancer with different stages were collected, histologically verified by a pathologist and analysed for the co-expression of miR-200c and DLC-1 using qRT-PCR. SKOV3 cell line was transfected with the miR-200c mimic, miR-200c inhibitor and nonspecific sequences that acted as the control group.
Results: In clinical samples, the expression of miR-200c was significantly up-regulated ($p<0.0001$) in the early and advanced stages compared to the normal. The expression of DLC-1 gene was down-regulated but it was not statistically significant. In SKOV3 cells treated with miR-200c mimic, the expression of DLC-1 was down-regulated but it was not statistically significant. In contrast, cells treated with miR-200c inhibitor resulted in significant up-regulation of DLC-1 ($p<0.0001$).
Conclusion: MiR-200c could promote metastasis by targeting and suppressing the expression of DLC-1 gene, and serve as promising therapeutic target in SEOC

FPP003

A RETROSPECTIVE ANALYSIS OF ADVERSE DRUG REACTIONS AMONG THE PATIENTS ATTENDING PRIMARY HEALTH CENTRES IN PETALING DISTRICT

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Aims: The objective of this study is to analyze the pattern of adverse drug reactions in a primary health center in Malaysia. It is also aimed to assess the causality and the severity of the adverse drug reactions.
Methods: This was a retrospective study based on case series analysis carried out with the data obtained from six primary health centres in Petaling district, Selangor. Ethical clearance was obtained for the study. The data of patients who attended the health centres between 01-01-2014 to 31-12 2014 were analyzed. The patients were analyzed for gender, age, type of drugs involved, the severity using Hartwig's severity assessment scale and causality using Naranjo ADR probability scale. Data was analyzed using descriptive statistics.
Results: A total 113 adverse drug reactions were reported. The mean age of the patients was 49.4±18.4 years. 67.3% of the patients were females and 32.7% males. Amlodipine was the commonest drug causing adverse drug reaction (20.4%) followed by amoxicillin (6.2%). The severity of the adverse reaction was commonly level 2 (69.9 %) followed by level 3 (21.2 %) as per Hartwig's severity assessment scale. According to Naranjo ADR probability scale for causality assessment, the adverse drug reactions were mostly found to be probable (48.7%) reactions. 61.9% of the patients recovered from the adverse drug reaction.
Conclusion: Amlodipine was the most common drug causing adverse drug reaction in patients under the study. Level 2 reactions were commonly noticed and the causality assessment was probable in most of the patients.

FPP004

THE EFFECT OF APOCYNIN AND CATALASE IN CYCLOSPORINE A-INDUCED RENAL INSUFFICIENY RATS: THE TOTAL ANTIOXIDANT CAPACITY APPROACH

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Aims: Cardiovascular and renal diseases are major and leading causes of morbidity and mortality. Both systems are interrelated and often prognosis of one terminates to other system. This study investigates the effect of apocynin, an NADPH oxidase inhibitor and catalase in cyclosporine A (CsA) induced oxidative stress in the pathogenesis of cardiovascular and renovascular system.
Methods: 48 males Wistar-Kyoto rats were randomly assigned into 8 groups (n=6) with group 1 to group 4 as the negative control model, group 5 to group 8 as renal insufficiency model. Renal insufficiency was produced in selected groups using CsA (25mg/kg/day p.o). Apocynin (2.5mmol/L p.o) and catalase (10000 $U \cdot kg^{-1} \cdot day^{-1}$, i.p. bolus) were administered into all the experimental models. Weekly non-invasive blood pressure, heart rate, metabolic data, renal functional and renal haemodynamic parameters were recorded. Oxidative stress markers, such as plasma malondialdehyde, superoxide dismutase, nitric oxide and total antioxidant capacity markers, were used to detect the degree of oxidative stress. Histopathological studies were also performed.
Results: Deterioration on renal functional parameters, blood pressure, heart rate, metabolic data, renal haemodynamics and oxidative stress markers were observed in CsA-treated rats. Renal tubular ischemia, mild arteriolar congestion and abscess inflammation were observed in the subcapsular region of CsA-treated rats. However, these phenomena were not observed in Apocynin and catalase-treated groups.
Conclusion: Apocynin and Catalase can be considered as a potential therapeutic option in future for CsA induced nephropathy condition.

FPP005

PROGESTERONE RECEPTOR ISOFORM EXPRESSION IN ENDOMETRIOSIS IN MALAYSIAN POPULATION

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Aims: This study aimed to determine the expression of progesterone isoforms in endometrioma as compared to the matched eutopic endometrium in endometriosis patients. It also compared the expression of progesterone isoforms in eutopic endometrium in patients with and without endometriosis.
Methods: This study was carried out in UKMMC from 1st December 2016 to 31st July 2018. Endometrial tissues were obtained from patients who underwent surgery for suspected endometrioma. The control group was taken among patients who underwent pelvic surgery for other purposes. Total RNA was extracted from histologically confirmed endometrial and endometrioma tissue. QPCR was carried out after Cdna conversion.
Results: A total of 16 patients of endometriosis and control (n=8 for each group) were analysed in this preliminary data. Quantitative PCR identified the Mrna expression of PRB was 4.0-fold higher in the ectopic tissue compared to only 2.1-fold in the eutopic tissue, but this was not statistically significant. A similar pattern was observed for PRA. The relative expression of Mrna of PRB was 1.5-fold higher in the ectopic tissue compared to 1.2-fold in the eutopic tissue which was also not statistically significant. The ratio of relative Mrna expression of PR-B:PR-A was 1.1-fold higher in the ectopic tissue which was similar with the eutopic tissue.
Conclusion: The trend of changes was consistent towards a higher perturbance in the ectopic tissue compared to the eutopic tissue in endometriosis patients. A larger sample size is required to confirm the significance. This may be of benefit in determining the response of progesterone-based therapy for treatment in patients with endometriosis.

FPP006

INVESTIGATION OF IN-VITRO EFFECT OF GLYCOSYLATED SULFONYLUREA ON INSULIN-DEPENDENT PATHWAY AND DIABETES LINK ENZYMES.

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Aim: Impairment in insulin signaling pathway has been found to be the main cause of insulin resistance. Skeletal muscle and some enzymes serve as crucial site for treatment of type2 diabetes. The focus of this study was to determine the effect of glycosylated sulfonylurea (GS) on diabetes link enzymes & reactive oxygen species (ROS) activity, and insulin-dependent signaling pathway in insulin resistance L6 skeletal muscle cell.
Methods: The inhibitory effect of GS on diabetic link enzyme and reactive oxygen spices, such as alpha glucosidase, alpha amylase, dipeptidyl peptidase IV enzyme, lipid peroxidation, DPPH, nitric oxide, hydroxyl, free scavenging activity was tested with GS following manufacturer protocol. Differentiated L6 muscle cells from Rattus norvegicus were induced insulin resistance with high insulin and glucose and treated with GS. Cell toxicity and the expression of PI3K, IRS-1, PKC, AKT2 and GLUT4 genes involved in insulin-dependent signaling pathway was evaluated using qPCR.
Results: GS showed an in vitro antidiabetic and antioxidant effect by inhibiting alpha glucosidase, alpha amylase, dipeptidyl peptidase IV enzymes, lipid peroxidation, DPPH, nitric oxide, hydroxyl, free scavenging. GS was not toxic to cell and IRS-1, PI3K, AKT2 and GLUT 4 was less expressed in the induced insulin resistance L6 muscle cells treated with saline, but was highly expressed in the group treated with GS.
Conclusion: GS possesses in vitro anti-diabetic and antioxidant activity. It prevented the impairment in insulin dependent signaling pathway by up-regulating the gene expression of IRS-1, PI3K, AKT2 and GLUT 4 in insulin resistance L6 muscle cell.

FPP007

LEPTIN ADMINISTRATION ENHANCES MNNG-INDUCED GASTRIC CHANGES IN STOMACH OF MALE SPRAGUE-DAWLEY RATS

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Aims: Prevalence of gastric cancer is reportedly higher in obese individuals and serum leptin levels are elevated in obese people. Leptin increases the proliferation of gastric cancer cells in vitro, but its effect in vivo has not been determined. This study investigated the impact of leptin in a rat model of N-methyl-N'-nitro-N-nitrosoguanidine (MNNG)-induced gastric adenocarcinoma.
Methods: Male, Sprague-Dawley rats, aged six weeks, were divided into Group 1 (control); Group 2 (24mg/kg/day of MNNG in drinking water); Group 3 (intraperitoneal injection of 60 g/kg/day of leptin); Group 4 (MNNG and leptin) with 8 rats per group. After 40 weeks of treatment rats were euthanized and stomachs were collected for histopathology, microarray analysis. Data were analysed using Fisher's exact test and one-way ANOVA.
Results: Leptin-treated stomachs showed hyperplasia (12.5%) and dysplasia (12.5%) and upregulation expression of transcription factors (Nupr1, Ybx1), oncogenes (Tmem134, Ptma), translation factors (Eef1a1, Eif4g2), cell proliferation (Reep5), vesicular (Tmed2) and membrane trafficking (Rab7a) genes. Microscopically, 75% of MNNG+leptin-treated stomachs showed gastric changes including hyperplasia, dysplasia, hypertrophy, and adenocarcinoma ($p<0.01$). Genes upregulated include microRNAs, olfactory and vomeronasal receptors, signal transduction (Pde4d), and cell proliferation (Lcn11). Gastric hyperplasia was observed in 50% of MNNG-treated stomachs ($p<0.05$), with no changes in gene expression.
Conclusion: Leptin significantly enhances MNNG-induced gastric hyperplasia, dysplasia, and hypertrophy in male Sprague-Dawley rats, which supports the potential role of leptin as a contributing factor to the increased risk of developing gastric cancer in susceptible obese individuals.

FPP008

A STUDY ON MAGNESIUM ACETYLTAURATE AND TAURINE AGAINST NMDA-INDUCED EXCITOTOXICITY ON RETINAL DAMAGE

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Aim: Excitotoxic retinal injury involving NMDA receptors is associated with activation of nitric oxide synthases (NOS); neuronal NOS (Nnos), inducible NOS (Inos) and endothelial NOS (Enos). This results in retinal nitrosative stress leading to apoptotic loss of retinal ganglion cells, the hallmark of glaucoma. Magnesium acetyltaurate (MgAT) is a combination of magnesium and taurine, both of which are known for neuroprotective properties. This study aimed to investigate if MgAT and taurine alone provide neuroprotection by restoring the retinal NOS expression.
Methods: MgAT was administered intravitreally to rat eyes. In pre- and post-treatment groups, MgAT or taurine were given 24 hours before and after NMDA, respectively. In co-treatment group, MgAT or taurine were co-administered with NMDA. One of the groups similarly received vehicle (PBS) while another NMDA.
Results: Immunohistochemistry revealed that Nnos and Inos expressions were significantly higher in NMDA group compared to vehicle-treated group ($p>0.001$). Nnos- ($p<0.001$) and Inos-positive cells ($p<0.05$) were significantly reduced in groups pre-treated with MgAT and TAU ($p<0.001$). Enos, expression was significantly reduced in NMDA compared to PBS group but was significantly greater in MgAT pre-treated group compared to NMDA group ($p>0.05$). Similar observations were obtained for all 3 NOS isoforms ($p<0.05$). However, the effects of MgAT were greater than TAU alone, particularly in pre-treated group.
Conclusion: MgAT and TAU prevent the death of RGCs loss by preventing the altered expression of all 3 NOS isoforms.

FPP009

A COMPARATIVE STUDY ON THE SAFETY AND EFFICACY PARAMETERS OF CYCLOSPORINE AND TACROLIMUS ON RENAL TRANSPLANTED PATIENTS: A MALAYSIA EXPERIENCE

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Aim: In this study, the clinical safety and efficacy of cyclosporine, tacrolimus and between tacrolimus formulations, Prograf® and Advagraf® is compared.
Methods: A retrospective review on clinical and laboratory parameters were conducted for cyclosporine and tacrolimus at 3-month, and then monthly at 6th to 12-month, at 2 years and 3 years were conducted. Similarly, data was also collected for tacrolimus formulations (Prograf® and Advagraf®) for both pre- and post-conversion. In addition, causality assessment of suspected adverse, biopsy proven acute rejection (BPAR) and patients and graft survival was also recorded.
Results: The mean cyclosporine and tacrolimus trough levels were within the recommended therapeutic ranges (189.16±69.10 ng/ml and 7.84±2.18 mg/day respectively). The mean survival rate was significantly longer ($p=0.03$) with cyclosporine-based treatment as compared to tacrolimus as shown by the Kaplan-Meier analysis. Following conversion to Advagraf®, the mean tacrolimus trough level and daily dose decreased significantly ($p<0.01$) from 6.11±2.15 to 4.91±1.25 ng/ml and 4.08±2.19 to 3.48±1.79 mg/day, respectively. HDL was significantly increased ($p=0.005$) while triglycerides was significantly decreased following conversion to Advagraf® ($p=0.003$). The incidence of BPAR was 16% (4 cases in Prograf® and 7 cases in Advagraf®). There were 34 cases of adverse events which were classified as certain (5%), probable (36%), possible (23%) and unlikely (36%) with no significant differences between groups.
Conclusion: Overall, cyclosporine and tacrolimus did not show any significant difference in terms of safety and efficacy parameters among renal transplanted patients. Furthermore, Advagraf® might have an advantage in terms of lipid profile.

FPP0010

DETERMINATION OF MODIFIABLE FACTORS ASSOCIATED WITH BONE HEALTH: AN EXPLORATORY STUDY IN MALAYSIAN ADOLESCENTS USING QUANTITATIVE ULTRASOUND

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Aims: Peak bone mass (PBM) is a critical determinant of bone health in adulthood. Determining modifiable predictors that affect bone accrual so as to optimize PBM may have long-term consequences for osteoporosis. This cross-sectional study aimed to explore the influence of body composition; body mass index (BMI), fat mass (FM), lean mass (LM) measured via bioelectrical impedance device, and multiple lifestyle factors; physical activity (PA), calcium, or combination of vitamin D supplement intake, smoking and alcohol drinking status assessed via questionnaire on bone health evaluated by calcaneus quantitative ultrasound (QUS).
Methods: A stratified random sampling design was employed to recruit 920 healthy secondary school adolescents aged 15-17 years. QUS measurements were performed at the left calcaneus and generated speed of sound (SOS), broad-band ultrasound attenuation (BUA) and stiffness index (SI).
Results: After adjusted for significant covariates, results from the gender-specific multivariable linear regression analyses indicate that PA was positively associated with all three QUS indices in both genders; BMI was positively associated with SI and SOS in females; LM was positively associated with BUA in both genders; and FM was negatively associated with SI in females. These predictors contributed for 15.4%, 23.6% and 17.2 % of males' BUA, SOS and SI variances ($p<0.001$), respectively and 21.2%,32.1% and 29.4% of females' BUA, SOS and SI variances ($p<0.001$), respectively.
Conclusion: Tailor-made intervention to increase PA, reduce FM and increase LM while aiming for a healthy BMI may increase bone accretion and subsequently PBM, a protective determinant against osteoporosis in adulthood.

FPP011

PHARMACOLOGICAL MODEL DEVELOPMENT FOR CHRONIC EPILEPSY-INDUCED COGNITIVE DYSFUNCTION IN ZEBRAFISH

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Aims: Zebrafish is one of the well accepted animal model for seizure-like conditions. Zebrafish is well explored for acute seizure condition using pentylenetetrazole (PTZ) and other proconvulsants, but there is no attempt to develop a kindling model in zebrafish. To best of our knowledge, the present study is the first study to develop a PTZ kindling model in zebrafish and also assess the cognitive status after chronic epilepsy.
Methods: Zebrafish were exposed to low-dose PTZ daily for 10 days. Seizure-like behavior is determined by seizure score stages, which are well established. Cognitive performance was evaluated using a 3-axis maze followed by Mrna expression of important genes.
Results: Kindling model was successfully developed in zebrafish which was supported by high seizure scores. The animals also exhibited significant impairment in cognitive functions like memory. Results were further supported by modulations in Mrna expression of important genes.
Conclusion: Chronic epilepsy model using PTZ kindling is developed in zebrafish and it is a better alternative for screening of potential drugs. This model is also an important tool to assess epilepsy-related cognitive dysfunction and impact of AEDs on cognitive functions.

FPP012

NEUROPROTECTIVE EFFECTS OF BRAIN-DERIVED NEUROTROPHIIC FACTOR (BDNF) AGAINST AMYLOID BETA1-40 PEPTIDE (Aβ1-40)-INDUCED RETINAL AND OPTIC NERVE INJURY

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Aims: Recently, it was discovered that amyloidosis-related alterations, similar to those seen in the brain of patients with Alzheimer Desease (AD), occur in the retina of glaucoma patients. These alterations were also identified in the retinas of AD patients. This study aimed to the investigate neuroprotective effects of brain derived neurotrophic factor (BDNF) against amyloid beta1-40 peptide (Aβ1-40) induced retinal and optic nerve injury.
Methods: In this study, the rats were divided into 3 groups and were given intravitreal injections. Group 1 (control group) was injected with vehicle (PBS); group 2 (Aβ1-40) was injected with 5 nmol Aβ1-40 while groups 3 were injected with 5 nmol Aβ1-40 in combination with BDNF. Fourteen days after injection, rats were sacrificed, eyes were enucleated, fixed and processed for H&E staining, TUNEL assay and Toluidine blue staining. The thickness, area and length of the inner retinal layer and ganglion cell layer was measured and the number of cells counted. Subsequently, morphometric analyses were performed.
Results: Severe degenerative changes were observed in retina after intravitreal Aβ1-40 exposure. Treatment with BDNF increased retinal cell survival ($p<0.05$). TUNEL assay showed decreased number of apoptotic signal in BDNF group by 8.97 folds ($p<0.01$) compared to Aβ1-40 group. The Toluidine blue stained optic nerve sections showed reduced signs of degenerations, such as vacuolation of cytoplasm and nuclei condensation, in BDNF treated group by 2.43 and 2.50 folds than in Aβ1-40 group ($p<0.01$).
Conclusion: Co-treatment with BDNF prevents RGC apoptosis induced by Aβ1-40.

FPP013

NEUROPROTECTIVE EFFECT OF RESVERATROL AGAINST COLLAGENASE-INDUCED INTRACEREBRAL HAEMORRHAGE IN RATS: A PRELIMINARY STUDY

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Aim: The most common cause of haemorrhagic stroke is intracerebral haemorrhage (ICH). Despite low incidence, it is often fatal due to the unavailability of neuroprotective treatment. Since trans-resveratrol has been shown to have neuroprotective properties, its effect on rats with ICH were elucidated in this study.
Methods: 24 male Sprague Dawley rats weighing 250-350 g were randomly divided into four groups (n=6): (i) control, (ii) sham, (iii) ICH pretreated with vehicle (0.1% DMSO saline, i.c.v.) and (iv) ICH pretreated with trans-resveratrol (0.9µg, i.c.v.). ICH was induced by intrastriatal collagenase (0.04 U) injection using stereotaxic apparatus. 48 hours after ICH, functional outcomes were assessed using variety of functional and behavioral tests such as open field, grip strength and rotarod motor test. Following functional and behavioral tests, rats were euthanized, and brain was subjected to gross evaluation of hematoma volume.
Results: Pretreatment with trans-resveratrol attenuated motor coordination deficits as demonstrated by open field test (improved tracking plot, increased total distance travelled by 5 folds, increased speed by 3 folds, increased rearing frequency by 8 folds, increased grooming frequency by 8 folds) as well as increased latency to fall off the rotarod as compared to vehicle-pretreated ICH group. Besides, gross evaluation showed reduced hematoma volume in trans-resveratrol pretreated group as compared to vehicle-pretreated ICH group. Additionally, trans-resveratrol pretreated group showed higher survival rate when compared to vehicle-pretreated ICH group.

Conclusion: Resveratrol exhibits a significant neuroprotective effect in rat model of ICH.

FPP014

NEUROPROTECTIVE EFFECT OF PLGA NANOPARTICLE-BOUND BDNF ON MIDDLE CEREBRAL ARTERY OCCLUSION (MCAO) MODEL OF ISCHEMIA IN RATS

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Aim: Poly(lactide-co-glycolide) (PLGA) nanoparticles (NPs) as biodegradable carriers is useful in transporting neuroprotective drugs across blood brain barrier (BBB). Targeted brain derived neurotropic factors (BDNF) delivery across BBB provides neuroprotection in brain injury. We tested neuroprotective effect of PLGA nanoparticle-bound BDNF (BDNF-NPs) on middle cerebral artery occlusion (MCAO) model of ischemia in rats.
Methods: Sprague-Dawley rats were divided into 4 groups of 7 rats each. Group 1 was subjected to sham operation, group 2, 3 and 4 were subjected to permanent MCAO (pMCAO). Four hours after pMCAO, group 3 and 4 were intravenously treated with BDNF and BDNF-NPs respectively. Functional outcome was assessed at 2 h and 24 hours after pMCAO using modified Neurologic Severity Score (mNSS), and rotarod. Following functional assessments, rats were sacrificed by terminal cardiac puncture, blood was taken for assessment of neurobiomarkers (NSE) level and brain was subjected for infarct volume measurement.
Results: BDNF-NPs treated group showed significant improvement in mNSS when compared with pMCAO and BDNF treated groups demonstrating decreased mNSS score by 2.0 and 2.1 times. BDNF-NPs treated group showed improved rotarod performance by increasing latency time on rotarod by 2.44 and 2.77 folds when compared with MCAO and BDNF treated groups. The infarct volume in rats treated with BDNF-NPs was significantly smaller by 1.91 and 1.95 folds when compared

with MCAO and BDNF treated groups. The results were further corroborated by the estimation of neurobiomarkers (NSE) level.

Conclusion: BDNF-NPs exhibit a significant neuroprotective effect in pMCAO model of ischemia in rats.

FPP015

NEUROPROTECTIVE EFFECT OF NANOPARTICLE-BOUNDED BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) ON EXPERIMENTAL HAEMORRHAGIC STROKE IN RATS

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Aims: Brain derived neurotrophic factor (BDNF) plays important roles in brain plasticity and repair. It shows neuroprotective effects in experimental models of ischemic stroke. This study was aimed to investigate neuroprotective effect of BDNF-loaded poly(lactic-co-glycolic acid) (PLGA) nanoparticles (NPs) on experimental haemorrhagic stroke (HS) in rats.
Methods: Sprague-Dawley rats were divided into 6 groups of 9 rats each. Group 1 was a sham operation while group 2, 3, 4, 5 and 6 were induced with HS. 15 minutes after induction, groups 1 and 2 were treated with saline; group 3 was treated with empty PLGA NPs; group 4 with PLGA NPs coated with surfactant; group 5 with BDNF-loaded PLGA NPs and group 6 with BDNF-loaded PLGA NPs coated with surfactant. Behavioral assessments (open field test, rotarod and grip strength test) were done before and after treatment on days 1, 3 and 7. On day 7, rats were sacrificed and brains were taken for histological and immunohistochemical analysis.
Results: Open field test showed that treatment with BDNF-loaded PLGA NPs (group 5 and 6) exhibited significant increases in rearing (number of times the animal stands on its hind legs) compared with other HS groups, which is often interpreted as an expression of directed exploration. BDNF NPs treated group showed improved rotarod performance by increasing their time spent on the rotarod. Rats treated with BDNF-loaded PLGA NPs also exhibited increased grip strength as evidence of motor neuroprotection.
Conclusion: BDNF-loaded PLGA NPs has neuroprotective effect on experimental haemorrhagic stroke in rats.

FPP016

INVESTIGATING THE ROLE OF AMPK PATHWAY IN LEPTIN-INDUCED ADVERSE EFFECTS ON SPERM PARAMETERS IN SPRAGUE-DAWLEY RATS

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Aim: The mechanism of leptin-induced adverse effects on spermatozoa is unknown. This study investigated the effects of dorsomorphin (AMPK inhibitor) on leptin-induced adverse effects on sperm parameters in Sprague-Dawley (SD) rats.
Methods: Male SD rats, weighing 400-450 grams, were divided into 3 groups. Group 1 was treated with 0.1 ml saline, Group 2 with leptin (60 µg/kg/day) and Group 3 with leptin+dorsomorphin (5 mg/kg/day) for 14 days intraperitoneally. Body weight and food intake were recorded on day 1 and day 14. Animals were euthanized on day 15. Sperm count, percentage of sperm with abnormal morphology, seminiferous tubular diameter and epithelial height, and 8-hydroxy-2-deoxyguanosine (8-OHdG) levels were determined.
Results: No significant difference was observed in body weight and food intake among the three groups. Sperm count was significantly lower in Groups 2 and 3 vs. Group 1. Percentage of sperm with abnormal morphology was significantly higher in Groups 2 and 3 vs. Group 1. No significant difference was observed in seminiferous tubule diameter. However, seminiferous tubule epithelial height was significantly lower in Groups 2 and 3 vs. Group 1. Levels of 8-OHdG were significantly higher in Groups 2 and 3 vs. Group 1.
Conclusions: Dorsomorphin, when given at a dose of 5 mg/kg/day, did not prevent the adverse effects of leptin on sperm parameters. Therefore, it can be concluded that either i) the dose and/or duration of dorsomorphin was insufficient, or ii) the AMPK pathway is not among the possible pathway(s) through which leptin exerts these effects.

FPP017

PROCYANIDIN-C1 MITIGATES BISPHENOL-A ADVERSE EFFECT ON SPERMATOGENESIS IN ADULT MALE MICE

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Aims: There is an increasing trend for men to have children at age over 35 years old. Increasing paternal age has been shown to affect the male fertility by reduction in sperm quality. Bisphenol-A (BPA) is an endocrine-disrupting chemical which is widely used in the production of polycarbonate plastics. It has been proven to impair spermatogenesis. However, procyanidin C1 (PCY-1), an antioxidant from Vitis vinifera L. has been shown to have antiviral and immunostimulatory effect. This study aimed to evaluate the effect of PCY-1 on spermatogenesis of BPA-treated adult mice.
Methods: Male C57BL/6 mice aged 4-6 months were divided into 4 groups (n=6). Males in the four groups were treated with ultrapure water (control), BPA (15mg/kg/bw), PCY-1 (20µg/kg/bw) and BPA 15mg/kg with 20µg/kg of PCY-1 respectively, for 35 days. The cauda epididymides and testes were collected on Day-36, for sperm parameter analyses and histomorphometry. Statistical significance was determined by one-way ANOVA with $p<0.05$
Results: In sperm parameter analyses, PCY-1 treatment significantly increased sperm morphology (48.00 ± 4.00 vs. 23 ± 1.0) compared with control group. Intervention of PCY in BPA+PCY group significantly increased sperm morphology (19.0 ± 1 vs. 11 ± 0.5) and sperm count (87.5 ± 2.5 vs. 57 ± 7.00) compared with BPA group. Histomorphometry showed that, PCY-1 treatment increased epithelial height (403.34µm$\pm$16.00µm) compared to control group (344.77 ± 11.00µm). In BPA+PCY-1 group the seminiferous tubule diameter significantly increased (629.59 ± 22.80µm) compared to BPA group (527.71 ± 6.73µm).
Conclusion: PCY-1 improves spermatogenesis in adult male mice exposed to BPA.

FPP018

EFFECT OF EXOGENOUS GLUTATHIONE (GSH) ON SPERM PARAMETERS IN STZ-INDUCED DIABETIC C57BL/6 MICE

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Aims: Increased oxidative stress in the testes and epididymis induces sperm DNA damage in most diabetic models. Glutathione (GSH) is a natural antioxidant which provides protection against oxidative damage. This study examined the effects of GSH on sperm parameters in STZ-induced diabetic mice.
Methods: Sixteen-week-old male C57BL/6 mice were randomly assigned to either treatment or control groups (n=6). Test mice were given multiple low-dose injections of streptozotocin (STZ) (50mg/kg/bw in 0.1ml Na-Citrate buffer) whilst control animals were injected with equivalent doses of the STZ vehicle. The diabetic state was determined a week after the final injection by blood glucose measurement. Non-fasting blood glucose and body weight were recorded weekly. Intraperitoneal injections of 30mg/kg GSH were given weekly for 42 days to the treatment groups. Sperm were collected from the cauda epididymis for evaluation of sperm count, motility, and abnormalities. Eosin-Y stained smears of fresh semen were used to evaluate sperm abnormalities. Data were analyzed using ANOVA.
Results: Sperm motility was significantly lower in the GSH-treated group compared to the controls ($p<0.05$). No significant difference was observed in sperm count compared to the control. Percentage of sperm with abnormal morphology was significantly higher in GSH-treated groups compared to the control group ($p<0.05$).
Conclusion: The dose and duration of GSH was insufficient to reverse the effect of diabetic on sperm parameters in diabetic induced C57BL/6 male mice. Further studies should look into the comparison of different doses of GSH on sperm parameters.

FPP019

PI3K PATHWAY INHIBITOR PREVENTS LEPTIN-INDUCED ADVERSE EFFECTS ON SPERM COUNT AND MORPHOLOGY

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Aim: Leptin has been shown to have adverse effects on sperm parameters, but the precise pathway remains unclear. This study therefore examines if LY294002 (a PI3K inhibitor) prevents leptin-induced adverse effects on sperm in Sprague-Dawley rats.
Methods: Sixteen-week old male Sprague-Dawley rats were given intraperitoneally for 14 days either: 0.1ml of normal saline (Control); or 60µg/kg/day of leptin (LEP); or 60µg/kg/day of leptin and 1.2mg/kg/day of LY294002 (LEP+LY). Animals were euthanized on Day 15. Total sperm count, percentage of sperm with abnormal morphology, seminiferous tubule diameter (STD) and epithelial height (STEH), level of 8-hydroxy-2-deoxyguanosine (8-OHdG) and pAkt/Akt ratio were determined. Data were analysed using ANOVA.
Results: Sperm count was lower in LEP when compared to control ($P<0.05$) and LEP+LY ($P<0.001$) groups. Fraction of sperm with abnormal morphology was higher in LEP than control ($P<0.05$) and LEP+LY ($P<0.01$). The pAkt/Akt ratio was higher in LEP ($P<0.001$) than control. Levels of 8-OHdG was higher ($P<0.05$) in LEP than control. STEH but not STD was lower in LEP than control ($P<0.01$). STEH was higher in LEP+LY ($P<0.001$) compared to control.
Conclusion: Administration of the PI3K pathway inhibitor, LY294002 (1.2mg/kg/day), prevents the adverse effects of leptin on sperm parameters and testicular tissue, which suggests the involvement of the PI3K signalling pathway in the adverse effects of leptin on sperm and testes.

FPP020

TRENDS IN THE PRESCRIBING OF SECONDARY PREVENTATIVE CARDIOVASCULAR THERAPIES IN MALAYSIAN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION AND CONCURRENT CHRONIC KIDNEY DISEASE

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Aim: Patients with higher risk of coronary disease may not receive optimum therapy, a phenomenon known as treatment-risk paradox. This study aimed to examine the prescribing trends of secondary preventative cardiovascular therapies in patients with acute myocardial infarction (AMI) with concurrent chronic kidney disease (CKD).
Methods: This is a retrospective cohort study of patients admitted with AMI to 18 Malaysian hospitals in the National Cardiovascular Disease Registry from 2006 to 2013 (n=30,873). Those with concurrent CKD were identified (n=3,194, 51% >65 years, 69% male and 52% Malay). Cardiovascular therapies examined were antiplatelets (aspirin and adenosine-diphosphate (ADP) receptor antagonists), angiotensin converting enzyme inhibitors (ACEIs)/angiotensin receptor blockers (ARBs), beta-blockers and statins. Adjusted odds ratio (OR) with 95% confidence interval (CI) were calculated using multivariate logistic regression. Linear trend test was used to examine prescribing over time.
Results: Of patients with both AMI and CKD, 74% had diabetes and 91% hypertension. The prescribing rates of preventative cardiovascular therapies were as follows; 83% aspirin, 74% ADP receptor-antagonist, 35% ACEIs/ARBs, 67% beta-blockers and 82% statins. Prescribing rates had increased over the study period ($p<0.0001$) including for ACEIs/ARBs (10% in 2006/2007, 53% in 2012/2013). Those with both AMI and CKD were less likely to receive aspirin (OR=0.59 [95% CI 0.41, 0.86], p=0.006), ACEIs/ARBs (OR=0.49 [0.37,0.63], $p<0.00001$) and statins (OR=0.54 [0.39,0.75], $p<0.00001$) compared to those with AMI but no documented CKD.
Conclusion: Patients who presented with AMI with CKD background were less likely to receive treatments such as aspirin, ACEIs/ARBs and statins although prescribing rates have been improving over the years.

FPP021

ROSELLE LIMITS EARLY CARDIAC REMODELLING IN RAT MODEL OF MYOCARDIAL INFARCTION

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Aim: Continuous loss of cardiomyocytes regulated by oxidative stress is a significant contributor to progression of post infarct cardiac remodeling and heart failure. Roselle (*Hibiscus sabdariffa*) calyces rich with natural polyphenols is well-known for its health benefits, yet its effects on early cardiac remodelling in post myocardial infarction (MI) setting are still unclear. This study aimed to investigate the actions of roselle extract on early cardiac remodelling in rat model of MI induced by isoprenaline.

Method: Male Wistar rats (200-300 g) were randomly allotted into 4 groups; control, roselle control, MI and MI with roselle. MI was induced with isoprenaline (ISO) (85 mg/kg, s.c) for two consecutive days followed by roselle supplementation (100 mg/kg, p.o.) for 7 days.

Results: MI was evident by elevation of troponin-T. Suppression of antioxidant level, such as total superoxide dismutase and total glutathione, and significant increase of thiobarbituric acid reactive substances, were seen in MI rats compared to control, indicating oxidative stress. Suppression of Bcl2 gene expression and upregulation of Bax gene expression were also seen in MI group. Consistently, significant upregulation of cytosolic cytochrome C protein expression suggested apoptosis in post MI rats. A relatively high percentage of collagen deposition showing fibrosis was observed in rat heart tissues of MI. Interestingly, roselle supplementation attenuated all these changes in MI subjected rat, except for the apoptosis markers.

Conclusion: In conclusion, these results showed that roselle limits early cardiac remodelling in rat model of MI by alleviating oxidative stress and fibrosis.

FPP022

POTENTIAL OF PIPER SARMENTOSUM AS AN ANGIOTENSIN CONVERTING ENZYME INHIBITOR IN CULTURED ENDOTHELIAL CELLS

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Aim: Over activity of angiotensin converting enzyme (ACE) has been implicated in the pathogenesis of hypertension. Piper sarmentosum (PS) is an herb with antihypertensive activity. This study aimed to elucidate the effect of PS on ACE level in cultured human umbilical vein endothelial cells (HUVEC).
Methods: HUVEC were divided into four groups: control, treatment with 200 µg/ml aqueous extract of PS, induction with an ACE inducer; 200 Nm phorbol 12-myristate 13-acetate (PMA) and concomitant treatment with PMA and PS for 24 hours. Subsequently, HUVEC were lysed and ACE protein level was measured using enzyme-linked immunosorbent assay (ELISA) while ACE activity was measured using colorimetric assay.
Results: Compared to control, induction of HUVEC with PMA caused an increase in ACE protein level (7.97$\pm$0.010 vs. 20.01$\pm$0.018 ng/mg protein, $P<0.05$) and ACE activity (1.86$\pm$0.064 vs. 3.68$\pm$0.061 nmol/ml/min, $P<0.05$). Treatment of PMA-induced HUVEC with PS reduced ACE protein level (20.01$\pm$0.018 vs. 13.75$\pm$0.011 ng/mg protein, $P<0.05$) and ACE activity (3.68$\pm$0.061 vs. 2.80$\pm$0.308 nmol/ml/min, $P<0.05$).
Conclusion: PS reduces ACE protein level and activity in HUVEC. Therefore, PS has the potential to be developed as an ACE inhibitor in the future.

FPP023

MARINOBUFAGENIN MIGHT BE INVOLVED IN LEPTIN-INDUCED INCREASES IN BLOOD PRESSURE AND MARKERS OF ENDOTHELIAL ACTIVATION DURING PREGNANCY IN SPRAGUE DAWLEY RATS

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Aim: The precise mechanism responsible for leptin-induced increase in blood pressure and proteinuria during pregnancy in the rat is unknown. This study examined the effect of resibufogenin (RBG), a marinobufagenin antagonist, on leptin-induced changes in blood pressure, markers of endothelial activation and proteinuria during pregnancy in the rat.
Methods: Four groups of Sprague-Dawley rats (n=8), aged 12 weeks were given either normal saline (Control) or 120µg $kg^{-1}day^{-1}$ of leptin (LEP), or 120µg kg^{-1} day^{-1} of leptin+30µg $kg^{-1}day^{-1}$ of resibufogenin (L+RBG) or 30µg $kg^{-1}day^{-1}$ of RBG from day 1 to 20 of pregnancy. Systolic blood pressure (SBP), body weight and urinary protein excretion (UPE) were measured at days 0 and 20. Animals were euthanized on day 21 of pregnancy and serum was collected for analysis of ACE2, VCAM-1, ICAM-1, E-selectin and endothelin-1. Kidneys and placentae were collected for histology and gene expressions of ICAM-1, endothelin-1 (ET-1) and ACE2.
Results: Compared to the Control, L+RBG and RBG groups, LEP had significantly higher SBP, UPE, ICAM-1, and ET-1 levels in serum, lower ACE2 concentration in the kidney, significantly higher ICAM-1 and ET-1 but lower ACE2 gene expression in the kidney, higher ET-1 but lower ACE2 gene expression in the placenta. No significant differences were found in any of these between Control and L+RBG, and RBG treated rats.
Conclusion: Prevention of leptin-induced changes in blood pressure, urine protein, and serum, kidney and placental parameters during pregnancy by RBG suggests the possible involvement of marinobufagenin in leptin-induced hypertension and proteinuria of pregnancy.

FPP024

ATTENUATION OF REMODELING IN DEXAMETHASONE PRETREATED HUMAN TRABECULAR MESHWORK CELLS BY TREATMENT WITH INHIBITORS OF RENIN-ANGIOTENSIN SYSTEM

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Aim: Dexamethasone causes extracellular matrix (ECM) remodelling in trabecular meshwork that leads to increased intraocular pressure. This study evaluated time and dose-dependent effects of RAS inhibitors on production and degradation of ECM in dexamethasone pretreated human TM (HTM) cells.
Methods: HTM cells were pretreated with dexamethasone 10^{-7}M for 14 days. Group-1 was cultured in Dulbecco's modified Eagle's medium (DMEM) only and group-2 with dexamethasone 10^{-7}M. The rest of the groups were treated with dexamethasone 10^{-7}M with either enalaprilat ehydrate or losartan potassium in concentrations of 10^{-4}, 10^{-5}, 10^{-6}, 10^{-7}M for both drugs. All groups were incubated for 7 and 14 days followed by detection of fibronectin (FN), α-smooth muscle actin (α-SMA), matrix metalloproteinases (MMPs) and tissue inhibitors (TIMPs) using immunocytochemistry and western blot.
Results: Dexamethasone significantly increased deposition of ECM and TIMPs. The levels of FN, α-SMA, TIMP-1 and TIMP-2 were 1.44, 2.30, 2.29, 1.70 folds higher compared to DMEM group on day 7 and 1.42, 1.52, 2.47 and 2.26 folds on day 14 after pretreatment; respectively. MMP-2 and MMP-9 secretions were significantly reduced by 1.99 and 2.33 folds on day 7, and 3.27 and 2.35 folds on day 14, respectively. Treatment with RAS inhibitors diminished the effects of dexamethasone on ECM by reducing the deposition of FN, α-SMA, and both TIMP-1 and TIMP-2 while increasing the MMP-2 and MMP-9 levels in all tested concentrations at both time points. No dose or time-dependent effects were found.
Conclusion: RAS inhibitors are effective for the treatment of steroid-induced glaucoma

FPP025

PROTEIN KINASE D2 AND ALDOSTERONE ACTIONS ON SODIUM CONSERVATION BY THE KIDNEY

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Aims: Aldosterone promotes Na+ conservation by the distal nephron through multiple mechanisms that include the transcriptional up-regulation of the epithelial sodium channel (ENaC) and Na^+/K^+-ATPase subunits and the activation of protein signalling pathways. The protein kinase D (PKD) family of serine-threonine protein kinases play a critical role in many cellular processes including the subcellular trafficking and membrane insertion of transport proteins. The aim of this study was to establish the role of PKD2 in the actions of aldosterone in the distal nephron.
Methods: Confocal microscopy was used to investigate the subcellular localization of PKD2 in M1 cortical collecting duct (CCD) cells. The effects of suppressing PKD2 expression on transepithelial short circuit currents (ISC) was measured in Ussing chamber-type apparatus.
Results: PKD2 is localized to the principal cells of the CCD. When PKD2 expression was suppressed in M1 CCD cells using shRNA, there was an increase in basal short-circuit current compared to wild-type cells. PKD2 knock-down also resulted in an increase in the amiloride-sensitive EnaC current (IEnaC) compared to wild-type. The effect of aldosterone on both ISC and IEnaC was abolished the under conditions of PKD2 knock-down. PKD1 and PKD2 play critical roles in aldosterone-induced EnaC activity.
Conclusion: PKD1 activation promotes EnaC membrane insertion, however PKD2 is a negative regulator of EnaC activity when present at the apical membrane. Aldosterone removes this "brake" on Na^+ uptake by activating PKD2 to cause its removal from the apical membrane and sequestration in the TGN.

FPP026

ULTRASTRUCTURE OF VITRIFIED MURINE EMBRYOS UNDER THE INFLUENCE OF MATERNAL ALPHA-TOCOPHEROL SUPPLEMENTATION

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Aims: Vitrification has become an important tool to store surplus embryos. However, cryoinjury from vitrification could affect preimplantation development. Studies have reported that tocotrienols in Vitamin E improves preimplantation development of murine embryos. To date however, there have been no reports on the effect of Vitamin E supplementation on embryonic vitrification outcomes. The aim of this study was to compare the ultrastructures of non-vitrified and vitrified embryos from females supplemented with Vitamin E.
Methods: The C57Bl/6 females were given oral gavage of 60 mg/kg/bw/day of corn oil stripped alpha-tocopherol (control), tocotrienol rich fraction (TRF) or alpha-tocopherol for 7 days. Two-cell embryos were equilibrated with EFS20 and vitrified with EFS40. Post warming viable 2-cell embryos were cultured in vitro for ultrastructural assessment. Embryos fixation with 2.5% glutaraldehyde was carried out before post-fixation with 1% osmium tetroxide. The samples underwent a dehydration series of graded acetone and infiltration with a series of resin mixture before staining with uranyl acetate, prior to viewing under the transmission electron microscopy (TEM).
Results: In non-vitrified groups, mitochondria were found distributed at the perinuclear region, to maintain cell metabolism. Meanwhile, in vitrified groups,

disruption of cellular membranes and poor structural intracellular preservation were observed. Lysosomes, and endoplasmic reticulum with mitochondria were found dispersed and clustered around cryo-damaged organelles. In the vitrified alpha-tocopherol group, lesser structural alteration was observed, contributing to better cryotolerance compared to other groups.

FPP027

METABOLOMIC CHANGES IN OVARY AND THE QUALITY OF OOCYTES RETRIEVED FROM AGING MICE FOLLOWING TOCOTRIENOL-RICH FRACTION SUPPLEMENTATION

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Aim: Aging is accompanied with an increased oxidative stress leading to a loss in ovarian function and eventually infertility. The beneficial effects of tocotrienol on female reproductive system have been proven. Metabolomic analysis was performed using ovarian tissue to determine the relationship between etabolomics changes in ovary and the quality of oocytes in aging mice following tocotrienol-rich fraction (TRF) supplementation.
Methods: Female *Mus musculus* mice were equally divided into four groups; i.e one group of six weeks old mice (Young, Group 1) and three groups of six months old mice (Aging, Group 2), vehicle control (Group 3) and TRF 150 mg/kg supplemented group (Group 4). After two months, mice from all groups were superovulated, and euthanized. Oocytes were collected and examined for its quality while ovarian tissues were collected for etabolomics analysis using LC/MS Q-TOF.
Results: The percentages of normal oocytes were significantly higher ($p<0.001$) and the fragmented oocytes were significantly lower ($p<0.001$) in TRF 150 mg/kg supplemented group as compared to vehicle control. Metabolomic analysis of the ovarian tissue showed that 26 metabolites were significantly different between Group 1 and Group 2, while 40 metabolites were significantly different between Group 3 and Group 4.
Conclusion: These data demonstrate that aging has a negative impact on cellular energy storage, energy metabolism and oxidative stress that subsequently affect female fertility. Supplementation with TRF reverses the changes on these metabolites and the affected pathways. Thus, it appears that TRF exerts a protective mechanism towards female reproductive aging.

FPP028

EFFECTS OF NICOTINE AND SUPPLEMENTATION OF TOCOTRIENOL RICH-FRACTION ON THE PI3K/ AKT SIGNALING PATHWAY IN PREIMPLANTATION MICE EMBRYOS

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Aims: Tocotrienol rich-fraction (TRF) is a potential reproductive protectant that may play important roles against birth defects during the regulations of embryonic development. The preimplantation embryonic growth is regulated by phosphatidylinositol-3-kinase (PI3K)/Akt signaling pathway. This study aimed to investigate the effects of nicotine and subsequent supplementation of TRF on the regulations of PI3K/Akt pathways in preimplantation embryos.
Methods: Twenty-four 6-8 weeks old (20-25g) female balb/c mice were randomly divided into four groups (G1-G4) and were treated for 7 consecutive days (Day 1-7): G1 (control) normal saline, G2 3 mg/kg/day nicotine (s.c), G3 both 3 mg/kg/day nicotine and 60 mg/kg/day of TRF and G4 60 mg/kg/day of TRF. On Day 8, animals were superovulated with 5 IU pregnant mare serum ganodotropin (PMSG) and 5IU human chorionic gonadotropin (hcG). Female mice were mated with fertile male and euthanized by cervical dislocation at 48 hours post-coitum. An embryo with 2 and 8 blastomeres from each group were collected. Embryonic DNA was purified and amplified for gene expression analyses.
Results: Exposure to nicotine induced DNA damage and dysregulation of PI3K/ Akt pathway possibly by downregulations of PTEN, Akt1, GSK3β and Mapk1 genes. However, supplementation of TRF on the nicotine-induced mice embryos up-regulated the expression of these genes. Intervention with TRF in G3 and G4 resulted in a significant upregulation of PTEN gene with 1.64-fold in G3 and 2.34-fold in G4. Similar pattern of expression was observed in Akt1, GSK3β and Mapk1 genes.
Conclusion: Intervention with TRF results in the embryonic cell proliferation and growth.

FPP029

A CASE-CONTROL STUDY ON MUSCLE STRENGTH OF MALE YOUTH WITH ARCHERY TRAINING

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Aim: Archery is an isometric game that combines muscular contraction-relaxation sequence during training, hence the training may promote muscle strength. This study aimed to investigate the differences in muscle strength between male youth involved in archery training and those who were not involved in any isometric training.
Methods: This is an aged-matched case-control study. Cases were healthy men aged 18-30 years in Klang Valley who underwent formal archery training for at least a year. Controls were selected from the general population of youth in Klang Valley without any formal or informal training of archery or isometric training. Assessment of subjects' muscle strength (Pound-force) was done using the JTech Commander Power Track MMT. Muscle groups assessed in this study included the shoulder, wrist, elbow, hip, and knee muscles. Data were analysed via independent t-test and chi-square with the level of significance was set at $p<0.05$.
Results: Forty male youth were included as cases and 73 as controls. Both groups fulfilled the inclusion and exclusion criteria of this study. The demographic and body composition data showed homogeneity characteristics between both groups ($p> 0.05$). Interestingly, the maximal force of muscle strength for upper and lower body in youth with archery training were significantly higher compared to the control group ($p< 0.05$).
Conclusion: Training of archery has a significant impact on muscle strength among youth, therefore the training deserves serious attention to be promoted as a leisure time activity with health benefits.

FPP030

THE EFFECT OF HYDROGEN-RICH WATER INGESTION ON EXERCISE-INDUCED MUSCLE DAMAGE

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Aims: Delayed-onset of muscle soreness (DOMS) and strength loss are the hallmarks of exercise-induced muscle damage (EIMD). This study investigated the protective effects of hydrogen (H_2)-water against DOMS and strength loss following EIMD.
Methods: In a randomized crossover manner, 11 adult males (24.0±3.9 years) received a 14-day treatment of either H_2-water or placebo, with a 28-day washout period between the trials. On the seventh day of the treatment, the participants undertook a 30-minute bout of downhill running (DHR) on a motorized treadmill at a speed corresponding to 65% of their VO2max and a slope of 15%. Assessments on DOMS and tenderness, range of motion, circumference of thigh, maximal leg extension strength, serum creatine kinase (CK) and plasma HSP70 were conducted before and repeated at various time points (0, 1, 2, 4, and 7 days) post DHR. Two-way repeated measures ANOVA was used to compare the changes of these variables between the trials. The area under the curve (AUC) and the peak values of these variables were also plotted and compared by paired t-test.
Results: DOMS and tenderness both increased within 2 days while muscle strength significantly impaired up to 4 days post-DHR. Blood CK and HSP70 increased at 1 and 2 days post-DHR, respectively. There were no treatment effects on these indices or blood markers of EIMD. However, AUC result showed that H_2-water treatment attenuated muscle soreness ($p=0.022$) and serum CK response ($p=0.033$) after the DHR. The peak serum CK value post-DHR was also lower ($p=0.029$) in the H_2-water trial.
Conclusion: Ingestion of H_2-water may reduce the DOMS and serum CK response following EIMD.

FPP031

ROLE OF K+ CHANNELS IN COLON EPITHELIAL WOUND HEALING

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Aim: The intestinal epithelium is renewed every 2-5 days. Evidence indicates that K^+ channels are key regulators of the migration and proliferation processes during epithelial restitution. This study aimed to determine the involvement of KCNQ1 and KCNN4 K+ channels in epithelial wound healing in colorectal cancer (CRC).
Methods: The HT29cl.19A cell line has a differentiated CRC phenotype, with robust expression of KCNQ1 and KCNN4. Scratch assays were used to study epithelial repair and cell migration following the inhibition of KCNQ1 with Chromanol 293B, and KCNN4 with TRAM-34. Single cell-tracking assays were used to measure cell migration 6, 12 and 24h after treatment with the selective channel blockers. Western Blotting was performed to determine the expression pattern of active β-catenin, cyclin D-1, ZO-1, KCNQ1 and KCNN4.
Results: KCNQ1 antagonism reduced wound healing at 24h (C293B: 38%±2.8) and at 48h (C293B: 60.6%±4.2). While KCNN4 inhibition increased the wound healing rate at 24h (TRAM-34: 62.7%±3.81) and at 48h (TRAM-34: 41.9%±1.77). Single cell tracking assays showed a time dependence in the effect of C293B. The effect was high at 6h (46.5%±1.9), decreased at 12h (25.0%±2.3) and increased again at 24h (60.4%±6.1). This revealed a cyclical expression of KCNQ1 during the first 24h of the epithelial repair process. The inhibition of KCNN4 with TRAM-34 up-regulated KCNQ1 protein expression, while cyclin D-1 protein expression was down-regulated.
Conclusion: The expression and functionality of KCNQ1 and KCNN4 K^+ channels are associated with wound repair and cell differentiation in CRC cells.

FPP032

ARE CADAVERS REAL HORRORS FOR MEDICAL UNDERGRADUATES? PHYSIOLOGICAL WAY OF THINKING

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Aim: Cadaveric dissection is a hallmark component of teaching and learning for Anatomy. Formalin is used across the medical schools as a preservative for the cadavers. Aim of this study was to find out the physiological manifestations of formalin vapour, reported by medical students associated with cadaveric dissection.
Methods: This descriptive study was carried out amongst the preclinical undergraduates of three different nationalities (Nepali, Indian and Sri Lankan) in the Manipal College of Medical Sciences (MCOMS), Pokhara, Nepal. The validated questionnaire administered to the students included the information regarding eye, ENT and skin related problems associated with dissection. Descriptive and inferential statistics used to analyse the data. Multivariate logistic regression expressed in odd ratios and 95% confidence interval (CI) was used to interpret the results.
Results: A total of 406 students were included in the study. The most frequent complaint was lacrimation 62.1%, CI [57.3, 66.7], ocular irritation 58.6%, CI [53.8, 63.3] and running or congested nose 42.1% CI [37.4, 47] at the time of dissection. Males experienced OR 1.403 (CI: 0.941, 2.091) times more running or congested nose than females during dissection. Disturbance in sight was reported by male student OR 1.48 (CI: 0.930, 2.356) times more than females.
Conclusion: Although clinical manifestations are linked with dissection in MCOMS, but they are comparatively less compared to other studies. Adopting suitable measures like using more exhaust fans, local exhaust ventilation system, short breaks in the session, protected measures like activated carbon mask, goggle and rubber glove will be helpful.

FPP033

THE EFFECTS OF REM SLEEP DEPRIVATION ON ENDOTHELIUM IN RAT MODEL

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Aims: Endothelial dysfunction is an early sign of cardiovascular disease. Sleep deprivation has been identified as a risk factor for cardiovascular disease. To date, the effects of sleep deprivation on endothelium remains poorly understood. This study aimed to evaluate the effects of REM sleep deprivation on endothelium in rat model.
Methods: Twenty-four male Sprague–Dawley (SD) rats were equally divided into 3 groups: free-moving control rats (FMC), REM sleep-deprived rats (REMsd) and tank control rats (TC). REM sleep deprivation was induced for 72-hour using the inverted flowerpot technique. Endothelium function was assessed using functional myograph study. The endothelium-nitric oxide synthase (eNOS) expression was measured using Western blot. In addition, scanning electron microscope (SEM) was used to assess ultrastructure of the endothelium.
Results: There was an impaired endothelium-dependent vasorelaxation to acetylcholine in REMsd rat. A vasomotion was also observed in REMsd rat aorta which was absent in both control groups (FMC and TC). eNOS expression was significantly lower in REMsd compared to FMC group. The endothelium surface of REMsd rat also showed features of endothelial damage as seen in SEM.
Conclusion: The above findings provide convincing evidence for the development of endothelial dysfunction in REM sleep deprivation. This endothelial dysfunction may contribute to increased risk of cardiovascular disease in sleep deprivation.

FPP034

MODULATING OF HOST PROTEINS EXPRESSION AS POTENTIAL MECHANISM OF ANTI-CHIKUNGUNYA VIRUS ACTION OF NOVEL 1-SUBSTITUTED 5-(PHENYLAMINO) URACIL DERIVATIVES ON VERO 76 CELLS

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Aim: Chikungunya virus (CHIKV) is a mosquito-borne alphavirus that causes fever and severe arthritis. The incidence of CHIKV infection has grown dramatically in tropical and subtropical countries while no specific treatment is available. Screening of 11 novel 1-substituted 5-(phenylamino) uracil derivatives revealed that compounds Z214 and Z364 possess inhibitory activity against CHIKV. This study aimed to identify possible mechanisms of anti-CHIKV effects for Z214 and Z364.
Methods: Vero cells were divided to Z214 and Z364 treated groups, virus control group and cell control group. All groups were incubated in T-25 flasks for 24 hrs. Total protein was collected using RIPA buffer and quantified. The samples were solubilized and loaded to IEF gel and subsequently SDS page. The gels were stained with Coomassie blue dye and the protein analysis was done using Progenesis same spot software. The proteins that were found to be significantly different ($p<0.05$) among the groups were subjected to mass spectrometry analysis.
Results: A total of 63 protein spots were selected for mass spectrometry and 50 known proteins were identified. Superoxide dismutase and NADPH oxidase were elevated in virus infected cells compared to non-infected cell group. Z214 and Z364-treated cells showed an increase of annexin A2 and peroxiredoxin 1 compared to CHIKV-infected group.

Conclusion: CHIKV infection induces inflammation associated with reactive oxygen species production. The antiviral mechanism of Z214 and Z364 is probably host-modulating in nature, associated with the increase of antioxidant proteins annexin A2 and peroxiredoxin 1 that regulate redox system and overcome cellular inflammation.

FPP035

THE EFFECTS OF TOPICAL APPLICATION OF POLYGONUM MINUS ESSENTIAL OIL ON DIABETIC WOUND HEALING

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Aims: Recent studies shows that Polygonum minus possesses anti-ulcer, anti-inflammatory, antioxidants and immunomodulatory activities. The aim of the present study was to determine the effect of topical application of Polygonum minus essential oil (PMEO) on the diabetic wound healing.
Methods: A total of 36 streptozotocin-induced diabetic male Sprague-Dawley rats were wounded. Four 6 mm full skin thickness wounds were created on the thoraco-dorsal aspect of the animals. The rats were then divided into three groups: non-treated (NT, n=12), topical application of silver sulfadiazine (SS, n=12), and topical application of PMEO (n=12). The rats were treated daily, until the day of sacrifice i.e. day 7 and 14 after wounding. The percentage of wound closure were calculated, and wound tissue were harvested for histological analysis.
Results: Percentage of wound closure on day 7 was better in SS to compare with NT and PMEO. On day 14, both SS and PMEO were better to compared with NT. Intact epithelium was only observed in both SS and PMEO on day 7, but on day 14, intact epithelium was present across all the groups, with dermal-epidermal interdigitations were apparent in both SS and PMEO groups. Collagen fibres were present abundantly in both SS and PMEO groups compared to NT.
Conclusion: PMEO promotes wound healing in diabetic wounds by increasing percentage of wound closure and promoting re-epithelialization and collagen fibre deposition especially after day seven.

FPP036

ISOFLAVONES IMPROVE BONE FORMATION IN BISPHENOL A INDUCED HFOB 1.19 CELLS VIA RANKL/OPG PATHWAY

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Aim: Soy isoflavones not only improve the osteoblast formation, but also has been ascribed to have potential effect on bone metabolism/function. Bisphenol A (BPA), an endocrine disruptor, disturbs the bone metabolism and interrupts the osteoblast function by increasing the RANKL and decreasing OPG expression. The present study aimed to investigate the direct effect of soy isoflavones (daidzein (Dz), genistein (Gt) and equol (Eq)) on the osteoblast cells, hFOB 1.19 cells, stimulated with BPA under RANKL/OPG pathway.
Methods: The molecular factors; RANKL, OPG and LRP-5 along with inflammatory markers and transcription factors were analysed via protein expression on hFOB 1.19 cells induced with BPA.
Results: Cells induced with 12.5µg/mL of BPA showed negative impact on the bone molecular mechanism. Following treatment with different concentration of isoflavones, there was increase cell viability in BPA induced hFOB 1.19 cells. It was observed that the suppression of RANKL, and expression of OPG and LRP-5 levels in isoflavones treated cells. Decreased inflammatory markers; IL-6 and TNF-α and increased Osx and Runx-2 were also observed.
Conclusion: Specifically, Dz-5 and Gt- 40µg/mL showed positive effect on bone formation under BPA exposure. Soy isoflavones directly improve the osteoblast formation under BPA exposure via RANKL/OPG pathway. Thus, soy isoflavones can be considered as alternative supplement for the treatment of bone loss due to BPA exposure.

FPP037

BONE-REPAIR GENES IN FRACTURED OSTEPOROTIC RATS TREATED WITH MARANTODES PUMILUM VAR. ALATA LEAVES

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Aims/Objective: *Marantodes pumilum var. alata* (MPva), a phytoestrogenic herb, promotes fracture healing in post-menopausal rats. This study aims to investigate the role of MPva on bone-repair genes during fracture healing in ovariectomized rats in an attempt to understand its underlying mechanism.
Methods: Five groups (n=6/group) of female Sprague-Dawley rats namely, Sham-operated (SO); ovariectomized control (OC); estrogen treatment (ET); 20mg leaf treatment (MP20) and 100mg leaf treatment (MP100) groups were studied. All rats, except the SO group, were ovariectomized to induce menopause. Eight weeks post-ovariectomy, the right tibiae of rats were fractured and immediately fixed with titanium plates. After osteotomy, ET received 64.5 g/kg/day oral dose of estrogen (Premarin®), MP20 and MP100 received 20mg and 100 mg/kg/day oral doses of MPva leaf extract, respectively, while SO and OC served as untreated controls. At the end of 8 weeks treatment, fractured tibiae were excised from euthanized rats and investigated for expression of bone repair genes (Bglap, Spp1, Dkk1, Igf1, Tnfsf11 and Fgf23) using QuantiGene plex assay. At $p<0.05$, results obtained were considered significant.
Results: Igf1 was significantly upregulated ($p<0.05$) in MP20 and MP100 while Tnfsf11 was significantly downregulated in MP20 ($p<0.05$). Dickkopf 1 homolog (Dkk1) was also found to be significantly upregulated ($p<0.05$) in all experimental goups compared to OC.
Conclusion: Bone fracture-repair property of MPva leaf extract may be attributed to its ability to induce an upregulation in expression of Igf1, a bone formation gene, and a corresponding downregulation in Tnfsf11, a bone resorption factor.

FPP038

BUNGA KANTAN IMPROVED BLOOD GLUCOSE CONTROL AND SUBSEQUENT RENAL-RELATED COMPLICATION IN DIABETIC RAT

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Aims: Renal failure secondary to diabetes has been a co-morbidity factor in uncontrolled diabetic patient. This study aimed to evaluate the effects of Bunga Kantan (Etlingera elatior flower) aqueous extract (BKAE) on diabetic profile and renal-related complications in streptozotocin (STZ)-induced diabetic rat's model.
Methods: Thirty male Sprague-Dawley rats were divided equally into 5 groups in this 12-weeks study. Group 1 was normal rat; Group 2 was untreated-diabetic rat; Group 3 was 500 mg/kg BKAE-treated diabetic rat; Group 4 was 1000 mg/kg BKAE-treated diabetic rat and Group 5 was 250 mg/kg metformin-treated diabetic rat. The effects of BKAE on blood glucose, body weight, and renal function were evaluated. Blood glucose and body weight were measured every two weeks. Kidney histology was evaluated using haematoxylin and eosin (H&E) staining.
Results: Twelve-week daily oral treatment with BKAE significantly reduced blood glucose level in diabetic rats. Concurrently, the BKAE also prevented body weight loss, as compared to untreated-diabetic rats. There was also a significant improvement in renal function parallel to structural morphology improvement.
Conclusion: Overall, the present findings showed that Bunga Kantan has anti-hyperglycaemic activity and may be used therapeutically to minimise the renal-related complications associated with diabetes.

FPP039

MALAYSIAN PROPOLIS, METFORMIN OR THEIR COMBINATION DOWN-REGULATES CASPASE-DEPENDENT APOPTOTIC SIGNALING AND INCREASES GERM CELL PROLIFERATION IN DIABETIC RAT TESTIS

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Aim: Diabetes mellitus (DM) has been reported to trigger apoptosis and decrease proliferation of testicular germ cells, both of which decrease male fertility potential. In the present study, we examined the effects of Malaysian propolis (MP), metformin (Met) and their combination, on apoptosis and proliferation of testicular germ cells in diabetic rats.

Methods: Thirty adult male Sprague-Dawley rats weighing 250-300g were divided into 5 groups (n=6/group) namely; normal control (NC), diabetic control (DC), diabetic+MP (MP at 300 mg/kg b.w./day), diabetic+Met (Met at 300 mg/kg b.w./day) and diabetic+MP+Met (D+MP+Met). DM was induced using a single intraperitoneal injection of streptozotocin (60 mg/kg b.w.). Treatment with the different interventions was done by oral gavage for 4 weeks.

Results: We found significant increases in mRNA transcript levels of p53 ($p<0.05$), Bax/Bcl2 ratio ($p<0.001$), caspase-8 ($p<0.001$), caspase-9 ($p<0.001$) and caspase-3 ($p<0.05$) in the testis of DC group, relative to NC group. Immunohistochemical staining of cleaved caspase-3 increased significantly ($p<0.001$), while proliferating cell nuclear antigen (PCNA) decreased significantly ($p<0.001$) in the testis of DC group, relative to NC group. Treatment with MP, Met, or their combination, significantly decreased mRNA transcript levels of the apoptotic markers, and resulted in a significant increase in PCNA immunostaining, with the best results observed in D+MP+Met group.

Conclusion: Malaysian propolis, metformin or their combination decreases apoptosis and increases proliferation of testicular germ cells in diabetic rats.

FPP040

MARANTODES PUMILUM (KACIP FATIMAH) IMPROVES HEPATIC INSULIN SIGNALING AND MUSCLE GLUCOSE UPTAKE IN OVARIECTOMISED DIABETIC FEMALE RATS

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Aim: Clinical trials and animal studies have revealed that loss of circulating oestrogen induces rapid changes in whole body metabolism, fat distribution, and insulin action. This study investigated the effects of *Marantodes pumilum* (MP) extract or locally known as kacip fatimah on the oestrogen receptor, metabolic characteristics and insulin signalling pathway in ovariectomised nicotidamide streptozotocin (n-STZ)-induced diabetes rats.
Methods: Female Sprague Dawley (SD) rats were randomly divided to into nine groups: Normal control (NC), Sham, Ovariectomised control (OVX), Ovariectomised diabetic rats (OVXS) treated with vehicle, OVXS with 50mg/kg and 100 mg/kg MP leaf aqueous extract, OVXS treated with 50 mg/kg and 100 mg/kg MP stem root ethanolic extract and OVXS treated with standard anti-diabetic agent, glibenclamide (600 g/kg) (OVXS+ Glib). Treatment were given by oral gavage for 28 days. Anti-diabetic effect, pancreas morphology, insulin signalling was evaluated by OGTT, ITT, histopathology, immunohistochemistry and western blot, respectively.
Results: Treatment with MP leaf aqueous and stem root ethanolic extracts significantly reversed the elevated fasting blood glucose, impaired glucose and insulin tolerance and lowered insulin content in the pancreas. MP treatment also prevented the decrease in hepatic estrogen receptors and proteins involved in insulin signaling in the liver and skeletal muscle.
Conclusion: Taken together, this study demonstrates that MP elevates estrogen receptor which may partly contribute to improved hepatic insulin signaling and glucose uptake in skeletal muscle in ovariectomised diabetic female rats.

FPP041

THE EFFECT OF *Jatropha gossypifolia* L LEAF ETHANOLIC EXTRACT ON TNF-α AND NEUTROPHILE COUNT IN RATS WITH INFLAMMED MUSCLE TISSUE

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Aims: This study aimed to prove the effect of the extract of *Jatropha gossypifolia* L leaves to TNF-α levels and neutrophil count on male Wistar rats were exposed carrageenan.
Methods: The design of this study is the post-test only control group design. The total sample size of 32 male Wistar rats aged 2-3 months, weighing 175-200 grams, were divided into 4 groups. Group K is a control, while the P1, P2, and P3 given extract of Jatropha gossypifolia L leaves orally for 3 weeks at a dose of 100 mg/kg, 200 mg/kg, and 300 mg/kg. On day 21, all groups were given injections carrageenan 1% 0.1 ml. Six hours after the injection, thigh muscle tissue was taken for estimation of TNF-α level and neutrophil count.
Results: TNF-α levels from the control group were significantly higher ($P<0.05$) compared to the group treated with the extract of *Jatropha gossypifolia* L leaves. Neutrophil count from the control group was significantly higher ($P<0.05$) compared to the group treated with the extract of Jatropha gossypifolia L leaves.
Conclusion: *Jatropha gossypifolia* L leaves have anti-inflammatory, indicated by decreased TNF-α and neutrophil counts.

FPP042

ANTI-INFLAMMATORY EFFECT OF 6-SHOGAOL DERIVATIVES ON LIPOPOLYSACCHARIDE-INDUCED INFLAMMATION IN SKELETAL MUSCLE CELLS

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Aim: 6-Shogaol, an active constituent of ginger has been reported to possess anti-inflammatory properties. Despite its potent anti-inflammatory effect, it has low bioavailability and low absorption through oral route. The present study was undertaken to investigate the anti-inflammatory effect of 6-Shogaol derivatives against lipopolysaccharide (LPS)-induced skeletal muscle inflammation.
Methods: The cytotoxicity of the 6-Shogaol derivatives against skeletal muscle cell was determined using WST-1 cell proliferation assay. The amount of IL-1β secreted by myotubes after LPS exposure was measured by ELISA. RT-qPCR analysis was used to determine interleukin-1β (IL-1β) and tumour necrosis factor (TNF-) mRNA expression.
Results: 6-Shogaol derivatives at various concentrations maintained the cell viability above 90% therefore proven non-cytotoxic to muscle cells. Myotubes treated with lipopolysaccharide neither expressed IL-1β mRNA nor secreted IL-1β protein. The level of TNF-α mRNA expression increased significantly in LPS-induced myotubes. 6-Shogaol derivatives at various concentrations significantly inhibited TNF-α mRNA expression.
Conclusion: 6-Shogaol derivatives exhibit exploitable anti-inflammatory properties and have a huge potential as an effective therapeutic agent for treating inflammatory myopathies.

FPP043

CHARACTERISTICS OF FRUCTOOLIGOSACCHARIDE FROM DIOSCOREA ESCULENTA AND ITS EFFECTS ON IMMUNE SYSTEM

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Aims: The aims of this study were to characterize the prebiotic activity of fructooligosaccharide (FOS) from Dioscorea esculenta and to determine its effect on level of sIgA, level of IL-10 and the phagocytic index in mice.
Methods: Fructooligosaccharide from Dioscorea esculenta was characterized based on its degree of polymerization and its ability to promote Lactobacillus sp and Bifidobacterium sp growth. Balb/c mice were supplemented daily with FOS from Dioscorea esculenta by gavage for 2 weeks. Secretory Immunoglobulin A (sIgA), Interleukin-10 (IL-10) was investigated by ELISA. The phagocytic index was quantified by direct observation using an inverted microscope for a total of three fields per well. Independent T-test was used to determine the mean difference between FOS and control group.
Results: Fructooligosaccharide from Dioscorea esculenta was shown to stimulate Lactobacillus sp and Bifidobacterium sp growth. The number of Lactobacillus sp and Bifidobacterium sp colony was higher in FOS group compared to control group ($p<0.05$). The levels of sIgA and IL-10 were significantly increased in FOS group than that of control ($p<0.05$). In addition, FOS group had a higher phagocytic index compared to control group ($p<0.05$).
Conclusion: This study concluded that FOS from Dioscorea esculenta as prebiotic with 2 and 5 degree of polymerization can up-regulate the level of sIgA, IL-10 level and phagocytic index in mice.

FPP044

IN VITRO EFFECT OF HIBISCUS YELLOW FLOWER EXTRACT AND CHINESE CABBAGE JUICE ON AMINOPYRINE METABOLISM IN RAT LIVER MICROSOMES

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Aim: Cytochrome P450 has been reported to interact with many drugs, food and herbal medicine. In particularly, CYP 3A4 is known to play a critical role in several relevant herb-drug and food-drug interactions. The objective of this study was to examine the in vitro herb-drug interaction of Chinese cabbage juice and methanol extract of Hibiscus yellow flower with aminopyrine metabolism in male Sprague Dawley rats.
Methods: The N-demethylation of aminopyrine catalyzed by CYP 3A4 in rat liver microsomes were examined by measuring the quantity of formaldehyde formed according to the colorimetric method.
Results: Chinese cabbage juice at 100 ng/ml ($p<0.01$) and 1000 g/ml ($p<0.01$) significantly reduced the CYP3A4 activity compared to the control group. On the other hand, a significant increase in the CYP 3A4 activity was observed in the rat liver microsomes treated with methanol extract of Hibiscus yellow flower at 1, 10, 100 and 1000 ng/ml ($p<0.01$) when compared to the control group.
Conclusion: Our findings suggested that Chinese cabbage juice and methanol extract of Hibiscus yellow flower could interact with the metabolism of aminopyrine in rat liver microsomes through the modulation of CYP 3A4 activity. Caution should be taken when these products are taken in combination with other therapeutic drugs metabolized by CYP3A4. Phytochemical analysis needs to be carried out to determine the constituents that present in both samples in this study.

FPP045

S-ALLYLCYSTEINE, A GARLIC ANTIOXIDANT, IMPROVES LEFT VENTRICULAR FUNCTION AFTER ISCHAEMIA-REPERFUSION INJURY IN RAT HEARTS EX VIVO

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Aim: Aged garlic extract and its derivative, S-allylcysteine (SAC) are effective against cardiomyocyte damage and oxidative stress. This study was undertaken to evaluate the impact of SAC on recovery of left ventricular (LV) function after experimental ischemia-reperfusion (IR) injury ex vivo.
Methods: Rat hearts were freshly harvested from Male Wistar rats (300-400g) and perfused retrogradely using Krebs-Henseleit (KH) buffer in Langendorff mode for measurement of LV pressure and its derivatives (±dP/dt). After steady state, each heart was subjected to 35-mins of global ischaemia and 60-mins of reperfusion. Rat hearts were given either KH buffer alone (IR control), or added with SAC (10 or 50 mM) throughout reperfusion, or sham control (n=4). At end of reperfusion, rat hearts were kept frozen and used for biochemical analysis.
Results: Compared to the sham controls, IR induced a significant reduction in LV developed pressure (LVDP), LV dP/dt and coronary flow (CF) throughout reperfusion (all $p<0.05$). IR also markedly increased LV end-diastolic pressure (LVEDP), an indicator of LV dysfunction compared to the sham controls ($p<0.05$). SAC (50 mM) significantly improved LVDP, LV dP/dt and CF, in addition to preventing IR-induced LVEDP elevation (all $p<0.05$). On biochemical analyses, SAC (50 mM) administration significantly attenuated total LDH release and oxidative stress associated with the IR injury as compared to the IR group (all $p<0.05$).
Conclusion: Our data altogether suggests that garlic antioxidant; SAC improves recovery of LV function after IR injury ex vivo. SAC might be beneficial for patients with myocardial infarction when given as adjuvant after reperfusion therapy.

FPP046

ANTIHYPERTENSIVE ACTIVITY OF FICUS DELTOIDEA KUNSTLERI IN SPONTANEOUSLY HYPERTENSIVE RATS: NMR-BASED METABOLOMICS APPROACH

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Aim: Chronic hypertension is a major risk factor for cardiovascular diseases. Ficus deltoidea var Kunstleri (FDK) was shown earlier to reduce blood pressure of spontaneously hypertensive rats (SHR). Since metabolomics helps uncover mechanisms associated with drug action, the metabolic changes in the urine of FDK-treated SHR was examined. The components of the renin-angiotensin-aldosterone system (RAAS) and endothelial function in the serum of SHR were also measured.
Methods: Three groups of male SHR were administered orally with either vehicle (group 1), or FDK 1000 mg/kg (group 2) or losartan 10 mg/kg (group 3) per day for 4 weeks. Twenty-four-hour urine was collected for NMR-based metabolomics analysis. At the end of week 4, blood was collected for the measurement of components of RAAS and endothelial function.
Results: Sera of FDK-treated SHRs had significantly lower concentrations of angiotensin I ($p<0.05$), angiotensin II ($p<0.05$) and aldosterone ($p<0.05$) but higher concentrations of angiotensin converting enzyme 2 (ACE2) ($p<0.01$) and nitric oxide synthase (eNOS) ($p<0.001$) when compared to those in the controls. A total of 48 metabolites were identified via metabolomics. Orthogonal partial Least Square-discriminant Analysis showed good separation and metabolic differences between FDK-treated and non-treated SHR. The discriminant metabolites were also identified for both groups. These metabolites are suggested to be involved in the RAAS as well as in endothelial function.

Conclusion: FDK extract exhibited a significant anti-hypertensive effect in SHR. Metabolites identified in the urine may contribute towards the understanding of the molecular mechanism of its anti-hypertensive effect.

FPP047

URINE METABOLITE CHANGES IN SPONTANEOUSLY HYPERTENSIVE RATS TREATED WITH FICUS DELTOIDEA ANGUSTIFOLIA: 1H NMR-BASED METABOLOMICS APPROACH

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Aims: Metabolomics provides a comprehensive insight into metabolite changes in diseases. Ficus deltoidea angustifolia (FDA) has been reported to reduce blood pressure in spontaneously hypertensive rats (SHRs). However, its effect on the urinary metabolites has not been investigated before. The aim of this study was to examine changes in urine metabolome following FDA supplementation in SHR using 1H NMR-based metabolomics approach.
Methods: Eighteen male SHR were administered orally once a day with either vehicle (group 1), or FDA 1000 mg/kg (group 2) or losartan 10 mg/kg (groups 3) for 4 weeks. Blood pressure was measured using tail-cuff plethysmography. 24-hour urine was collected at the end of the study for NMR-based metabolomics analysis
Results: Blood pressure was significantly lower in FDA and Losartan treated rats ($P<0.01$). A total of 48 urinary metabolites were identified that were different from the control following FDA administration. The significantly increased metabolites after FDA treatment included hippurate, taurine, dimethylamine, creatine, TMAO, methylamine, benzoate, allantoin, homocysteine. However, acetoacetate, lysine, lactate and pyruvate were decreased.
Conclusion: FDA extract decreased blood pressure in SHR with significant changes in some of the urinary metabolites. Metabolites identified in the urine may contribute towards the understanding of the molecular mechanism involved in the anti-hypertensive effect of FDA.

FPP048

ANTIHYPERTENSIVE AND URINARY METABOLICS CHANGES IN SHR TREATED WITH FICUS DELTOIDEA TRENGGANUENSIS (FDT) EXTRACT

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Aim: The leaves of Ficus deltoidea are often used in traditional medicine for the treatment of a number of ailments, including hypertension. However, evidence about its antihypertensive activity remains undetermined. This study was done to examine in vivo antihypertensive properties of FDT on spontaneously hypertensive rats (SHR) and evaluate their urinary metabolic changes.
Methods: Thirty male SHR, aged 12 to 14 weeks, weighing 200-300 g with systolic blood pressure (SBP) >150 mmHg were divided into groups receiving 1200 mg/kg bw of standardized aqueous-ethanolic extract of FDT, 10 mg/kg bw of Losartan or 0.5 ml of distilled water (n=6). They were force-fed orally daily for 4 weeks. Urine was collected weekly and assessed via the 1H NMR-based metabolomics approach.
Results: Systolic blood pressure was significantly lower ($p<0.05$) in the group treated with 1200 mg/kg bw FDT compared to controls. A total of 48 metabolites were identified. The current results highlighted the metabolic changes between untreated and FDT-treated groups at week 4. The metabolic profiles that were increased included dimethylamine, creatinine and citrate. However, metabolites, such as lysine and methylamine were decreased. Lysine showed a significant decrease when the rats were treated with FDT. Hippurate, benzoate and creatine which were upregulated in week 4, were also higher in the untreated and FDT-treated groups.
Conclusion: FDT extract significantly decreases blood pressure in SHR and the mechanisms involved are suggested by urinary metabolites. The pathways suggested should be determined to illustrate the underlying molecular mechanism of FDT in treating hypertension.

P01

UPA AND TPA MEDIATE TRANS-RESVERATROL-INDUCED OCULOHYPOTENSION

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Aims: Elevated intraocular pressure (IOP), the most important risk factor for glaucoma is due to increased deposition and lack of degradation of extracellular matrix (ECM) at the trabecular meshwork (TM). trans-resveratrol (TR) reduces IOP, however the mechanisms remain unknown. Tissue and urokinase plasminogen activator (tPA and uPA) convert plasminogen to plasmin, which increases ECM degradation. The study aims to elucidate the increased of tPA and uPA as the mechanism of TR-induced oculohypotension.
Methods: The in vivo study used Sprague-dawley rats (n=12) pretreated with dexamethasone to induce oculohypertension. Subsequently, Group 1 and Group 2 received vehicle and topical TR, respectively. After 1.5-hour the animals were sacrificed and uPA and tPA levels in the aqueous humour were estimated. The in vitro study used human TM cells that were incubated with 25 M of TR or vehicle for 1.5-hour. The media were collected to measure uPA and tPA.
Results: Topical TR treatment elevates AH uPA and tPA level by 1.9- and 1.5-fold compared to Group 1 ($P<0.05$), respectively. uPA concentration in the TR-treated culture media was 1.7-fold and tPA concentration was increased by 1.1-fold compared to vehicle treated group ($P<0.05$).
Conclusion: TR-induced IOP-lowering effect is associated with elevated AH and uPA and tPA level in culture media. The elevated levels correlated with the observation of IOP-lowering effect with topical TR treatment in rats occurring at 1.5-hour post single drop administration.

P02

OCULAR PENETRATION OF TOPICAL LIPOSOMAL AND MICROEMULSION FORMULATION CONTAINING LIPOPHILIC SUBSTANCE

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Aims: Topical application of drug for ocular disease is the most preferred route of administration. However, it is challenging due to presence of anatomical-physiological barriers that lowers the drug bioavailability. For a lipophilic substance to be delivered topically, it needs to be solubilized in aqueous form. Colloidal drug delivery system (CDDS), such as liposome and microemulsion formulations, solubilizes lipophilic substances. Besides, CDDS also provides sustained and controlled release of drug to targeted tissue. In this study, we compared the ability of topically applied to deliver lipophilic fluorescent dye, 1,1′-dioctadecyl-3,3,3′,3′-tetramethylindocarbocyanine perchlorate (DiI) to ocular tissues.
Methods: Sprague-Dawley rats were divided into 3 groups which received topically applied DiI in liposome (DL), microemulsion (DM) or dimethyl sulfoxide (DMSO) solution (DS). The eyedrop was given to unilateral eye, whereas the contralateral eye remained as control. Animals were euthanized at different time points post-instillation. Eyeballs were dissected and underwent frozen sectioning. Fluorescence intensity (FI) was measured on ocular tissues using
Leica LAS AF Lite 2.0 software.
Results: Higher FI for DL was observed in cornea at 10 and 30 minutes post instillation compared to DM and DS ($p<0.001$). Significant FI for DM was detected in ciliary body and retina from 10 until 120 minutes post-instillation compared to DL and DS ($p<0.05$). Comparable FI was seen between DL and DM in the retinal layers of contralateral eyes at 30 and 120 minutes post-instillation.
Conclusion: Significant and consistent ocular tissue distribution is seen with microemulsion formulation, whereas, systemic absorption of these two formulations is comparable.

P03

EXOGENOUS GLUTATHIONE ENHANCES PREIMPLANTATION EMBRYONIC DEVELOPMENT

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Aim: Preimplantation embryonic development can be perturbed by visible light, high oxygen concentration and metal cations. The perturbations are mediated through increased production of reactive oxygen species (ROS) which is known to cause serious dysfunction during preimplantation development. Glutathione is the major non-protein sulphydryl compound in mammalian cells which confer protection against oxidative damage. The objective of this study is to compare in vitro development and morphological quality of murine embryos cultured with and without glutathione (GSH).

Methods: Female mice were superovulated and embryos were harvested at 46-48 h. A total number of 187 embryos were selected and divided for culture in medium supplemented with and without 0.01 Mm GSH. Embryonic development and morphological grading were observed at 48, 72, 96 and 120 h.

Results: Development to the 8-cell, morula and blastocyst stages were significantly increased ($p<0.01$) in culture medium supplemented with GSH compared to control (76.6% vs 57.9%, 69.4% vs 44.7%, 69.4% vs 38.2% respectively). Significant improvement ($p<0.01$) in morphological quality was also observed in GSH cultures (72% vs 58%, 32% vs 28%, 18% vs 8% at 8-cell, morula and blastocyst were respectively at grade A stage).

Conclusion: 0.01Mm exogenous glutathione medium supplementation

significantly improved developmental competence and morphological quality of preimplantation embryos, probably due to the ability of GSH in maintaining the redox balance.

P04

FECAL MICROBIOTA PROFILE IN GROWTH-STUNTED CHILDREN

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Aims: This study aimed to compare the fecal microbiota profile of children with and without stunted growth.
Methods: The compotition of fecal microbiota from children with and without growth growth-stunted was assesed using culture based-method (n = 20; age 2–3 years). Independent t-test was performed to analyze the mean difference between two groups.
Results: the children with growth disorders had a significantly higher number of *Escherichia coli*, which was 9 fold higher than that of healthy counterpart. However, there was a significant number of *Lactobacillus sp*, which was 3 fold higher in healthy children than that of children with stunted growth.
Conclusion: Higher number of *Escherichia coli* and *Lactobacillus sp* may be associated with stunted growth among the Javanese children.

P05

EFFECT OF ANNATTO TOCOTRIENOL ON BODY COMPOSITION AND SERUM ADIPONECTIN, LEPTIN AND GLUCOSE LEVEL IN A RAT MODEL OF ANDROGEN DEFICIENCY INDUCED BY BUSERELIN

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Aims: Androgen deprivation therapy could lead to obesity. Annatto tocotrienol is reported to reduce the expression of genes related to adipogenesis but the mechanism remains elusive. This study aimed to evaluate the effects of annatto tocotrienol on body composition (lean and fat mass), serum adiponectin, leptin, and glucose levels in male rats treated with buserelin.
Methods: Thirty-two male Sprague Dawley rats aged 3 months old were divided randomly into four groups. The normal control (n=8) received corn oil (the vehicle of tocotrienol) orally daily and normal saline (the vehicle of buserelin) subcutaneously daily. The remaining groups received subcutaneous buserelin injection (75 µg/kg) daily. Buserelin group (n=8) was given corn oil orally, while treatment groups were given AnTT at 60 mg/kg (n=8) and 100 mg/kg (n=8) orally. The rats were euthanized after the three-month treatment. Dual energy x-ray absorptiometry was performed to measure the lean and fat mass of the rats. Blood was collected for the evaluation of adiponectin, leptin and glucose level using immunoassays.
Results: At month 3, the lean mass, fat mass, adiponectin and leptin levels for all groups increased significantly compared to their baseline values irrespectively of their treatment ($P<0.05$). All groups except AnTT 60 mg/kg experienced a significant increase in glucose level after 3 months ($P<0.05$).
Conclusion: Androgen ablation and annatto tocotrienol does not influence body composition, adiponectin and leptin levels in male rats. However, annatto tocotrienol at 60 mg/kg may improve glucose metabolism.

P06

PREVALENCE OF GLUCOSE INTOLERANCE AND DIETARY INTAKE IN WOMEN WITH PREVIOUS HISTORY OF GESTATIONAL DIABETES MELLITUS

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Aim: Reproductive age women with previous history of gestational diabetes mellitus (GDM) are at risk of developing type 2 diabetes mellitus (T2DM). However, prevalence of glucose intolerance and dietary intake in post GDM women remained to be evaluated. The aim of this study was to investigate the prevalence of glucose intolerance and dietary intake of post GDM women who are at risk of T2DM.
Methods: Demographic data and postpartum oral glucose tolerance test (OGTT) results of 18 post GDM women were recorded. Dietary intakes were obtained through three-day dietary recall from seven participants and evaluated using computerized dietary analysis program.
Results: The prevalence of glucose intolerance in post GDM women was 50% (impaired glucose tolerance (IGT), 38.9%; T2DM, 11.1%). Most women with glucose intolerance were Malays (77.8%) and 55.6% required insulin during pregnancy. There was no significant difference in demographic characteristics between post GDM women with and without glucose intolerance. The average daily calorie intake and macronutrients in post GDM women with glucose intolerance were within normal limit but the fiber intake was below Malaysian Dietary Guidelines recommendation (1447 $\pm$ 404 kcal/day, 54 $\pm$ 8.5% carbohydrate, 32 $\pm$ 6.2% fat,14 $\pm$ 2.8% protein and 6.3 $\pm$ 4 g/day fiber).
Conclusion: Prevalence of glucose intolerance in post GDM was high in women required insulin during pregnancy. Although not significant, dietary fiber intake was inadequate in post GDM women with glucose intolerance. Future research on a larger scale is warranted to obtain a significant outcome.

P07

CYTOGENETICALLY NORMAL ACUTE MYELOID LEUKAEMIA (CN-AML) CANCER-RELATED PATHWAY AND ITS INTERACTION ASSESSED BY HUMAN CLINICAL AND COMPUTATIONAL DATA

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Aim: The association between the dysregulated MicroRNA (miRNA) expression and cancers is well documented. However, there is a gap in our knowledge surrounding miRNA-Mrna interactions, specifically in miRNA's target (genes) and their pathways. The current study attempts to address this problem in cytogenetically normal acute myeloid leukaemia (CN-AML) by integrating both transcriptomic and microRNome data from experiment and bioinformatics.
Methods: Differential expressions of both miRNA and Mrna were measured and correlated. MiRNA-Mrna correlations were referred to miRNA target prediction databases. Predicted miRNA-Mrna interactions were selected and interrogated. MiRNA-Mrna pairs that were not predicted but showed direct significance to CN-AML were also selected. Gene ontology and network analysis were conducted to further understand the miRNA target genes biological functions and possible pathways involving them.
Results: Experimental analysis showed that the miR-199b-5p:GZMB interaction was highly correlated ($r=-0.91$) and significant ($p<0.01$). Interestingly, the same interaction was predicted by the database ($p<0.01$). The GZMB gene encodes proteins used by natural killer (NK) cells and cytotoxic T lymphocytes (CTLs) to induce cancer cell apoptosis, whereas miR-199b-5p is reported to be closely associated with CN-AML in numerous study. Other significant interactions shown in our study included 11 miRNA-Mrna pairs involving three AML genes; FLT3, MPO, and RUNX1 ($p<0.05$).
Conclusion: The current study showed some novel interactions between miRNA and Mrna targets with miR-199b-5p:GZMB being the potential interaction.

P08

AN EVALUATION ON CONSUMERS' PERCEPTION AND PRACTICE OF PARACETAMOL USAGE

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Aims: Paracetamol is a major constituent of many over-the-counter (OTC) drugs. Hepatotoxicity due to paracetamol overdose is a common problem in Malaysia. This study aimed to evaluate the knowledge and usage of paracetamol among the out-patients visiting the government clinics in Ipoh.
Methods: A cross-sectional descriptive study with convenient sampling was done. The sample size calculated was 184, and we recruited 200 for our study. Institutional approval was obtained. Data were collected from self-directed questionnaires consisting of three parts related to socio-demography, knowledge and practice on use of paracetamol. The questionnaires were distributed to respondents and completed with face- to-face interview. Associations between socio-demographic variables with knowledge were tested by using Chi-square test.
Results: Among the 200 respondents, males were 63 (31.5%) and females were 137 (68.5%). Age range varied from 18 to 70 years. With regard to the knowledge, 51.5% had good while 48.5% had poor knowledge. Males showed poor knowledge compared to females but the difference was not significant statistically.
Conclusion: Gaps in consumers knowledge leads to misuse and accidental overdosage of paracetamol. Necessary steps need to be taken to minimize the overdose of paracetamol.

P09

VITAMIN E ISOMERS PROMOTE BONE FORMATION AND TRABECULAR STRUCTURE OF BOVINE BONE SCAFFOLD

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Aims: Vitamin E is a strong antioxidant and has been demonstrated to improve bone structure, and offers beneficial effect against osteoporosis. This study aimed to determine osteocalcin level and bone structure in a 3-D bone model treated with tocotrienol isomers (α-, β-, γ-, δ-tocotrienol) and α-tocopherol.
Methods: hFOb 1.19 cells were seeded in bovine bone scaffold at a density of 2x106 per scaffold, and incubated overnight in growth media, DMEM F12 and 10% fetal bovine serum. The cells were exposed to individual tocotrienol isomers (α-, β-, γ-, δ-tocotrieonol) and α-tocopherol at concentrations of 100 nM. Osteocalcin expression was tested at day 7, 14 and 21. The undecalcified bone scaffold was sectioned and stained using Von Kossa staining.
Results: The osteocalcin levels for the bone scaffolds treated with tocotrienol isomers increased in a time-dependent manner and peaked at day 15. The levels of osteocalcin were higher in the cells treated with γ- and δ-tocotrienol compared to the other tocotrienol isomers. Bone structural histomorphometric analysis showed that the bone scaffolds treated with γ- and δ-tocotrienol showed significant increased bone surface, bone parameter, trabecular thickness and bone volume compared to other groups.
Conclusion: γ- and δ-tocotrienol showed the best results in terms of trabecular structure and enhancement of osteoblast mineralization as indicated by the osteocalcin expression.

P10

A NEWLY DESIGNED AND CHARACTERIZED BOVINE BONE SCAFFOLD PROMOTE GROWTH OF HUMAN OSTEOBLAST-OSTEOCLAST CO-CULTURE CELLS IN STATIC 3-DIMENSIONAL CO-CULTURE SYSTEM

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Aims: This study aimed to test the application of native bone scaffolds as a three-dimensional construct mimicking the endogenous skeletal microenvironment system.
Methods: A bone scaffold was prepared from bovine femoral trabecular bone and demineralized using 0.6 N hydrochloric acid. The native bovine bone scaffold was cultured with human foetal osteoblasts 1.19 (Hfob 1.19) and human peripheral blood mononuclear cells for 21 days under standard culture conditions (37°C, 95% humidity and 5% carbon dioxide). The porosity of the scaffold was determined by scanning electron microscope. Cells attachment on the scaffold was determined using a scanning electron microscopy. Histological evaluation was used to examine calcium deposition on the trabecular and dual-energy x-ray absorptiometry analysis was carried out to obtain the total bone mineral density (BMD) and bone mineral content (BMC) of the scaffold.
Results: Attachment and proliferation of cells, as well as mineralization of the scaffold, were shown to be successful. These caused increments in the trabecular thickness and trabecular number and the narrowing of the trabecular separation.
Conclusion: A native bovine bone scaffold seeded with bone cells is a promising tool to create living tissue constructs that are structurally, functionally and mechanically comparable to the natural bone.

P11

INTERLEUKIN 33 (IL33) MODULATION PRODUCED SIGNIFICANT IMPACT ON MALARIA PATHOGENESIS IN MICE

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Aim: Malaria affects millions of people throughout the tropical and subtropical areas of the world. Eradication of malaria is difficult due to drug and insecticide resistance. Until now, no effective vaccine is available for the disease. This study aimed at investigating the potential of interleukin 33 (IL33) modulation as an immunotherapeutic approach in dealing with malaria. IL33 functioned either as pro- or anti-inflammatory mediator in various diseases.
Methods: Plasmodium berghei ANKA infection in ICR mice was used as a model of malaria. Local and systemic release of IL33 were determined during the infection by means of immunohistochemistry and ELISA methods respectively. Modulation of IL33 during the infection was carried out by treatment of infected mice with either recombinant IL33 (rmIL33), neutralizing monoclonal IL33 antibody (mIL33ab) or recombinant IL-33 receptor ST2 Fc chimera (rmST2Fc).
Results: IL33 was significantly elevated in the plasma of malarial mice and was positively correlated with parasitaemia development. Immunohistochemistry revealed significant local expression of IL33 in the brain, lung and spleen tissues. Treatment with rmIL33 which augmented the endogenous levels of IL33 produced better survival rate among malarial mice and improved the severe histopathological features in various organs. Antagonizing and neutralizing IL33 levels by treatment with rmST2Fc and mIL33ab respectively produced lower survival rate and worsened the histopathological features of malarial mice.
Conclusion: Results suggest the crucial role of IL33 during malaria and augmenting its release during the infection may prove beneficial for the host. It may serve as a potential immunotherapeutic target in malaria.

P12

THE NOVEL MOLECULAR IMAGING MARKERS OF 18F-FLUOROCHOLINE PET/CT AND THE EXPRESSION OF CD47, miRNA-21 and miRNA-155 IN UNDERPINNING BREAST CANCER PATIENTS

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Aim: ^{18}F-Fluorocholine uptake increases during malignant transformation and potentially identifies the aggressiveness of cancer cells. However, the novelty of the ^{18}F-FCH and the expression of miRNA and CD47 were sought as there were limited reports on their role in underpinning aggressive breast cancers. We examined the ability of ^{18}F-FCH uptake and the expression of CD47 and miRNA in detecting aggressiveness of breast cancers.
Methods: Twenty-one breast cancer patients with BIRADS 4 or 5 on mammogram criteria were recruited and underwent ^{18}F-FCH PET/CT. Histological results were used as the gold standard. The standardized uptake value (SUV max) was analysed to determine the degree of altered choline metabolism on Positron Emission Tomography. The expression of miRNA was measured using quantitative real-time polymerase chain reaction. After the PCR cycles, melting curve analyses were performed to validate the specific generation of the expected PCR product by looking at the upregulated (miRNA expression) or downregulated (low miRNA expression). The CD47 expression was analyzed by using ELISA and the standard curve was constructed using regression analysis.
Results: This study showed that there is significant correlation between high SUVmax of ^{18}F-FCH with expression of miRNA-21 in lymph node and metastasis ($p=0.05$).While there is also significant correlation between high SUVmax of ^{18}F-FCH with expression of miRNA-155 in lymph node ($p=0.01$). Furthermore, there is a significant correlation between high SUVmax with expression of CD47 in lymph node ($p=0.008$).
Conclusion: ^{18}F-FCH and the expression of miRNA and CD47 are novel predicting markers in underpinning aggressive breast cancers.

P13

IN VITRO CHARACTERIZATION AND IN VIVO PERFORMANCE OF MEFENAMIC ACID-SODIUM DIETHYLDITHIOCARBAMATE BASED LIPOSOMES

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Aims: Mefenamic acid (MFA) is a hydrophobic drug with low dissolution rate. This study aimed to develop stable and reproducible aqueous formulations of MFA using liposomes as drug carriers.
Methods: The drug entrapment, particles size and drug release profiles, and stability and reproducibility of the liposomes were determined. In addition, the maximum tolerated dose (MTD) was determined in rats via the oral and intraperitoneal routes of administration. Also, the anti-inflammatory efficacy of these liposomes was evaluated using carrageenan-induced paw edema model in rats.
Results: MFA-DDC based liposomes demonstrated a drug entrapment efficacy of 93.6%, particles size of 170.9 nm, and polydispersity index of 0.24 which were not statistically affected when stored in room and refrigerated temperatures for at least 4 weeks. The MTD of the intraperitoneally administrated MFA-loaded liposomes was 20 mg MFA/kg, whereas for those of oral administrations, it was up to 80 mg MFA/kg. Intraperitoneal dose (80 mg MFA/kg) of MFA-DDC liposomes induced extrapyramidal symptoms associated with significant elevation in serum potassium and muscle enzymes. Moreover, significant inhibition of paw edema was demonstrated by the oral and intraperitoneal routes.
Conclusion: These findings suggest that MFA-DDC based liposomes are an effective formulation of MFA and recommend the use of bioequivalence assessments with commercial formulations.

P14

ANTI-INFLAMMATORY EFFECTS OF 6-THIOGUANINE (6TG) AND 6-HYDROXY-2-MERCAPTOPURINE (6H2MP) ON RAW 264.7 AND HIG-82 CELLS

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Aim: Rheumatoid arthritis (RA) is a chronic inflammatory and systemic auto-immune disease causes the loss of joint function and morbidity. Activation of immune cells leads to the mediator secretion of pro-inflammatory cytokines thus amplifying the inflammation. The 6-thioguanine (6TG) and 6-hydroxy-2-mercaptopurine (6H2MP) are purine nucleoside analogues, used in anti-tumor and in the treatment protocols of childhood acute leukemia's currently. No remarkable report has been made on the anti-rheumatic and anti-inflammatory effects of 6-thioguanine and 6-hydroxy-2-mercaptopurine. In this study, the anti-inflammatory role of 6TG and 6H2MP were evaluated in LPS-induced RAW264.7 cells and PMA-induced HIG-82 cell. The inhibition of PGE2, TNF-α, IL-1 and IL-6 production were measured in both cell types.
Methods: The supernatants from the cultures of RAW264.7 cells and RA fibroblast-like synoviocytes (RA-FLS) were treated with different concentrations of 6TG (6.25, 12.5 and 25 μM) and 6H2MP (25, 50, 100 μM) for 30 minutes before the incubation period of 24 hours with lipopolysaccharide (LPS, 25ng/ml) and phorbol myristate acetate (PMA, 10ng/ml) respectively. These supernatants are assayed for prostaglandin (PGE2), TNF-α, IL-1 and IL-6.
Results: 6TG and 6H2MP inhibited PGE2, TNF-α, IL-1 and IL-6 production in LPS-induced RAW264.7 cells and PMA-induced HIG-82 cell by concentration-dependent manner, thus 6TG was more effective than 6H2MP in low doses.
Conclusion: Overall results indicate that 6TG was more effective than 6H2MP in anti-inflammatory activity against induced inflammatory cytokines and lipid mediators, such as TNF-α, IL-1, IL-6 and PGE2.

P15

ANTINOCICEPTIVE ACTIVITY OF 2-BENZOYL-6-(3-BROMO-4-HYDROXYBENZYLIDENE)CYCLOHEXEN-1-OL IN FORMALIN-INDUCED PAW LICKING TEST

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Aims: 2-benzoyl-6-(3-bromo-4-hydroxybenzylidene)cyclohexen-1-ol (BBHC), a novel compound from the diarylpentanoid analogues, had shown significant antinociceptive activity in the acetic acid-induced abdominal constriction test as in the previous study. Hence, the current study was aimed to investigate the possible central and peripheral involvement in BBHC's antinociceptive activity in mice.
Methods: Male ICR mice were subjected to formalin-induced paw licking test. The mice were pre-treated with BBHC (0.1, 0.3, 1.0 and 3.0 mg/kg, i.p.) 30 min before the 2.5% formalin injection (20 µl, i.pl.). Control animals received only the vehicle (i.p.) while acetylsalicylic acid (100 mg/kg, i.p.) and morphine (5 mg/kg, s.c.) were used as the reference drugs. The mice were placed immediately in an individual observation chamber. The amount of time that the mice spent licking the injected paw, considered as indication of pain, was recorded for 30 min following formalin injection.
Results: The formalin-induced paw licking behavior was significantly suppressed by BBHC (0.1, 0.3, 1.0 and 3.0 mg/kg, i.p.) in both neurogenic (first phase) and inflammatory phases (second phase). BBHC was observed to inhibit neurogenic pain better than the inflammatory pain at all doses, especially at 3.0 mg/kg, where BBHC was found to exhibit 63.47% of inhibition ($p<0.001$) against neurogenic pain.
Conclusion: BBHC showed significant antinociceptive activity at both central and peripheral levels.

P16

CHANGES IN THE BODY WEIGHT OF MALE WISTAR RATS AT VARIOUS STAGES OF ALCOHOL ADDICTION

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Aims: Liquid diet is considered as one of the most appropriate techniques to reproduce chronic effects of alcohol in rodents owing to the route of administration and nutritional adequacy in the diet.
Objective: To evaluate the effects of ethanol-containing modified liquid diet (MLD) on changes in the body weight of male Wistar rats.
Methods: Seven-weeks-old male Wistar rats (n=18) with initial weight at the range of 200-300 g were allocated into three different groups: control, acute and chronic ethanol. The control group was fed solely with MLD (without ethanol) which included low fat milk powder, maltodextrin and sucrose for 27 days. Acute group was given control MLD for 27 days and ethanol (2.5 g/kg, 20% v/v in saline) was administered once on day 28 via intra peritoneal route. For chronic group, MLD without ethanol was given for first 7 days and followed by gradual introduction of ethanol at 2.4% (3 days), 4.8% (3 days) and 7.2% (14 days). Parameters such as body weight (g), MLD intake (ml) and ethanol intake (g/kg) were measured daily.
Results: At the end of MLD feeding, control rats weighed 8.66% higher than their initial weight. Similarly, the acute group also recorded an increase in weight, by 3.45%. The ethanol-fed rats in the chronic group weighed 15.40% lesser than their initial weight and each of them consumed an average of 14.16 g/kg day^{-1}.
Conclusion: No mortality was reported among the ethanol fed animals, supporting the appropriateness of the MLD for chronic alcohol rodent models.

P17

EFFECTS OF KELULUT HONEY ON BONE HISTOMORPHOMETRY IN GLUCOCORTICOID-INDUCED OSTEOPOROTIC MALE RATS

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Aim: The incidence of osteoporosis are in keeping with the rising number of old populations and also the use glucocorticoid to treat chronic illness. Long-term glucocorticoid use contributes to the pathogenesis of osteoporosis due to oxidative stress. The purpose of this study was to determine the effects of kelulut honey against glucocorticoid induced osteoporosis.
Methods: In this study, 62 male rats were used. Thirty-two adrenalectomized (Adrx) rats were divided into four groups; Adrx+Dex+NS, Adrx+Dex+Ca, Adrx+Dex+KH1 and Adrx+Dex+KH2 and was given normal saline 0.9% (control), calcium water (positive control), kelulut honey (KH1=400 mg/kg/day, KH2=200 mg/kg/day) treatment respectively. All of them were administered with intramuscular injection of dexamethasone (Dex) 120 µg/kg/ day. Twenty-four sham operated rats were given vehicle palm olein 0.05 ml/kg/day by intramuscular injection and 0.1 ml/kg/day orally. The remaining 6 rats become baseline group. After two months of treatment, the rats were euthanized. The femoral bones were tested for bone histomorphometry.
Results: Bone histomorphometry showed significant reduction in the bone volume/tissue volume (BV/TV) and trabecular number (Tb.N) of the femoral bones after two months of receiving dexamethasone treatment. Kelulut honey supplementation preserved The BV/TV, Tb.N and Tb.Sp of the rats receiving dexamethasone.
Conclusion: These results suggested that kelulut honey may have protective effect against glucocorticoid-induced osteoporosis. It may be used on patients receiving long-term glucocorticoid as prophylaxis to prevent osteoporosis.

P18

TOCOTRIENOL PROVIDES PROTECTION AGAINST GLUCOCORTICOID INDUCED OSTEOPOROSIS VIA REGULATION OF GENE EXPRESSION

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Aim: Glucocorticoids accelerate bone resorption while inhibiting bone formation. This study aimed to determine the regulation of gene expressions in glucocorticoid induced osteoporosis.
Methods: 32 adult male Sprague-Dawley rats were used in this study. 24 rats were adrenalectomized and divided randomly into 3 groups. They were administered with intramuscular dexamethasone injection 120 µg/kg/day. The Adrx+Dex+TT group was supplemented with annatto tocotrienol 60 mg/kg/day and the Adrx+Dex+ATF group with alpha-tocopherol (ATF) 60 mg/kg/day while the Adrx+Dex group was given vehicle palm olein 0.1 ml/kg/day by oral gavage. The sham operated rats (SHAM) were given vehicle palm olein 0.05 ml/kg/day by intramuscular injection and 0.1 ml/kg/day orally. The rats were euthanized after two months. Gene expressions were analyzed using the femoral bone homogenates and the tibias were analyzed for structural parameters of bone histomorphometry by micro computed tomography (MicroCT).
Results: Dexamethasone treatment significantly reduced total bone volume (TBV) and trabecular number (Tb.N) and increased trabecular separation (Tb. Sp) compared to the SHAM group. Cortical bone volume (CBV), trabecular bone volume (BV/TV) and trabecular thickness (Tb.Th) were not significantly changed. Treatment with tocotrienol (Adrx+Dex+ATT) maintained the TBV and the CBV, BV/TV and resulted in higher Tb.Th. Treatment with alpha-tocopherol did not result in significant changes. There were significant changes in the bone formation and and resorption gene expressions in both the Adrx+Dex+ATT and Adrx+Dex+ATF groups.
Conclusion: Tocotrienol shows better protective effects than alpha-tocopherol and can be used as a prophylaxis against glucocorticoid induced osteoporosis.

P19

THE EFFECTS OF FICUS DELTOIDEA ON BONE METABOLISM IN POST-MENOPAUSAL OSTEOPOROSIS RAT MODEL: A PRELIMINARY STUDY

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Aim: Postmenopausal osteoporosis occurs where there is a reduction in the bone mass due to cessation of ovarian functions, predisposing postmenopausal women to skeletal fractures. Plant-based supplements have been shown to be effective in preventing diseases associated with oxidative stress, including osteoporosis. Ficus Deltoidea, locally known as Mas Cotek, contains high amounts of polyphenols which are powerful antioxidants. Previous studies have reported its medicinal properties that include antidiabetic, anticancer, antibacterial and anti-inflammatory effects. However, to date, no reports have been made on its effects on bone metabolism. In this study, we investigate the effects of this plant extract on bone mass in ovariectomized rats.

Methods: In this preliminary study, 12 ovariectomized female Wistar rats were divided randomly into 4 groups. Three groups of rats were given different doses of Ficus deltoidea extracts (200 mg/kg, 400 mg/kg, 800 mg/kg body weight) while the remaining rats were given deionized water. The treatment period was 56 days and the extracts were administered using oral gavage. At the end of the study, the bones were analysed using the dual-energy x-ray absorptiometry machine.

Results: Rats treated with Ficus deltoidea extract at 800mg/kg showed a significantly higher bone mineral content compared to control group.

Conclusion: Ficus deltoidea was effective in preventing bone mineral loss in postmenopausal osteoporosis rat model

P20

THE EFFECTS OF TOCOTRIENOL ON BONE STRUCTURAL HISTOMORPHOMETRY, REMODELLING MARKERS AND HORMONES IN AN OSTEOPOROTIC RAT MODEL INDUCED BY METABOLIC SYNDROME

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Aims: This study aimed to investigate the effects of tocotrienol from Elaeis guineensis (oil palm) and Bixa orellana (annatto seed) on bone microstructures, remodelling markers, and hormones in male rats.
Methods: Forty two twelve-week-old male Wistar rats were divided into seven groups (n=6/group). The baseline group was sacrificed at the onset of the study. The normal group was given standard rat chow. The remaining five groups were fed with high-carbohydrate high-fat (HCHF) diet. At week 8, the five groups of animals fed with HCHF diet received tocopherol-stripped corn oil (vehicle), 60 mg/kg palm tocotrienol, 100 mg/kg palm tocotrienol, 60 mg/kg annatto tocotrienol, and 100 mg/kg annatto tocotrienol respectively. At the end of the 20-week study, the rats were sacrificed. Femur was harvested for the evaluation of bone structural analysis. Blood was collected for the measurements of bone remodelling markers and hormonal levels.
Results: The animals fed with HCHF diet had significantly lower bone volume, trabecular thickness, and significantly higher CTX-1 level compared to the animals fed with standard diet ($p<0.05$). For hormonal changes, HCHF diet significantly increased levels of leptin, insulin, and decreased adiponectin in male rats ($p<0.05$). Administration of palm and annatto tocotrienol significantly increased bone volume, trabecular thickness, and reduced serum leptin level in the HCHF rats ($p<0.05$).
Conclusion: Tocotrienol can prevent bone loss due to MetS, possibly by reducing the leptin level in male rats.

P21

THE EFFECTS OF NARINGIN ON BONE METABOLISM

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Aim: Osteoporosis is a skeletal disorder characterized by loss of bone mass and micro-architectural deterioration of bone tissues, leading to increased risk of fracture. Studies have shown that plant-based flavonoids could improve bone strength and mass while preventing the bone thinning. Naringin is a flavonoid which is predominately found in fruits and vegetables. This systematic review aimed to investigate the effects of naringin on bone metabolism, specifically on osteoporosis.
Methods: A literature research was done on the effects of naringin on osteoporosis animal model and tissue culture studies using electronic database (Ovid Medline, Ebsco Host and Scopus). Specific descriptors, i.e. "naringin OR osteoporosis OR bone OR bone loss", were used to perform the search.
Results: 10 articles, 3 from Ovid Medline, 5 from Ebscohost and 2 Scopus that complied with inclusion and exclusion criteria were selected. Based on the chosen articles, naringin has ability to increase the bone growth factors and prevent bone resorption.
Conclusion: Naringin has the potential to be used as a therapeutic agent for the treatment of osteoporosis.

P22

THE INFLUENCE OF HEART RATE TOWARDS PHOTOPLETHYSMOGRAPHY PARAMETERS FOR CARDIOVASCULAR DISEASE RISK ASSESSMENT: A REVIEW

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Aims: Finger photoplethysmography (PPG) waveform is the blood volume change of the finger microcirculation that reflects vascular function. Reflection index (RI) and stiffness index (SI) derived from PPG waveforms are proposed as cardiovascular disease (CVD) markers. Heart rate (HR) is a known factor affecting vascular function. Individual resting HR variation may affect RI and SI. This review aims to identify relevant studies about relationship between HR, RI and SI among healthy subjects.
Methods: Literature search was conducted in Medline via Ebscohost and Scopus databases to find relevant articles published in between 2008 to 2018. The main inclusion criteria were articles in English discussing the relationship between HR, RI and SI using PPG among human. The search found five articles that met the inclusion criteria.
Results: Out of five studies, only two studies observed significant association between SI and HR, and the associations were weak. The results were; r=0.28 (P=0.0006) and r=-0.06 (P=0.02). Out of four studies, three studies observed negative associations between RI and HR, and the associations were weak to moderate. The results were; r=-0.4 (P<0.001), r=-0.31 (P=0.001) and r=-0.35 (P<0.001).
Conclusions: The effect of heart rate towards SI are not consistent. A few studies

demonstrated significant but weak relationship between SI and HR. The relationship between HR and RI was consistent with weak to moderate associations. Further interventional studies should be conducted to investigate this issue as variation in resting HR may challenge the validity of PPG-based CVD markers.

P23

ASSOCIATION BETWEEN TESTOSTERONE AND CARDIOVASCULAR RISK MARKERS AMONG URBAN MALAYSIAN MEN

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Aims: Elderly men are at risk to suffer from age-related decline in testosterone level. This is accompanied by reduced sexual ability, fatigue, depression, cognitive impairment, osteoporosis, sarcopenia as well as increased risk for cardiovascular diseases. Pulse wave velocity (PWV) and augmentation index (AI) as markers of cardiovascular (CV) risk also increase with age. The studies on the relationship between testosterone and these CV markers are still lacking. The study aimed to determine the association between testosterone and CV risk markers among urban Malaysian men.

Methods: 335 men aged more than 39 years old were recruited from Klang Valley, Malaysia. Their body mass index (BMI), blood pressure (BP), pulse wave velocity (PWV), augmentation index (AI), high sensitivity C-reactive protein (HsCRP) and free testosterone (FT) were measured.

Results: The mean age of the subjects was 54.45±9.77 years old. Other results were as follows; BMI=25.46±4.26 kg/m^2, systolic blood pressure (SBP)=141.78±20.12 mmHg, diastolic blood pressure (DBP)=85.64±11.08 mmHg, PWV=8.55 ±1.38 m/s, AI=16.33±5.74%, HsCRP= 2.24±3.65 mg/L and FT=0.37±0.12 nmol/l. After adjustment for the age, FT was correlated with BMI ($r=-0.29$, $P<0.01$), SBP ($r=-0.15$, $P<0.01$) and HsCRP ($r=-0.14$, $P<0.05$). FT was an independent variable of AI (Beta=-0.14, $P<0.05$).

Conclusions: Testosterone is associated with markers of CV diseases. Age-related decline in testosterone may be responsible for increased CV diseases among aging men.

P24

THE CARDIOPROTECTIVE EFFECTS OF GYNURA PROCUMBENS (GP) SUPPLEMENTATION ON ISOPRENALINE-INDUCED MYOCARDIAL INFARCTION (MI) IN A RAT MODEL

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Aim: Gynura procumbens (GP) is known to possess medicinal properties such as antihypertensive, antihyperglycaemia, antioxidant and antimicrobial. This study aimed to evaluate the cardioprotective effect of oral administration of ethanol extract of GP on the isoprenaline-induced MI on lactate dehydrogenase (LDH), malondialdehyde (MDA) and components of the myocardial antioxidant defense system such as superoxide dismutase (SOD), catalase and glutathione peroxidase (GPx).
Methods: A total of 24 adult male Sprague-Dawley rats were used and divided into four groups (n=6); the control group (C), control group treated with GP 250 mg/kg (GP 250), MI untreated group (MI) and MI treated with GP 250 mg/kg (MI+GP 250). The rats were given 250 mg/kg GP supplementation or vehicle orally daily for 28 days. MI was induced by subcutaneous injection of isoprenaline on day 27th and 28th. On day 29th, the rats were sacrificed, blood samples were collected and heart tissues were harvested for investigations.
Results: Isoprenaline-induced MI was proven via the increased serum level of LDH, MDA, and the decreased activity of SOD, catalase and GPx. Administration of GP 250 mg/kg showed significant reduction of LDH and MDA level ($p<0.05$), whereas the activity of SOD and catalase significantly increased ($p<0.05$). However, no significant difference in GPx activity was observed.
Conclusion: The supplementation of GP 250mg/kg in isoprenaline-induced MI has shown to have cardioprotective effects in terms of increasing the antioxidant activities.

P25

THE EFFECTS OF QUERCETIN ON CARDIAC FUNCTION IN POST-ISCHEMIC-REPERFUSION CARDIAC INJURY AND PRESSURE OVERLOAD IN ANIMAL MODELS: A SYSTEMATIC REVIEW

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Aims: Ischemic cardiac injury and prolonged pressure overload can cause deterioration of cardiac function. Flavonoids have been demonstrated to be beneficial in improving cardiac function, in experimental studies. This systematic review aimed to evaluate the effects of quercetin, a flavonoid on cardiac function in post-ischemic-reperfusion injury and pressure overload animal models.
Methods: A search on articles was done systematically via Scopus, PubMed, Ovid and Ebscohost Medline, to select relevant studies on quercetin and cardiac function up to February 2018.
Results: The effects of quercetin on cardiac function in both models were reported in 9 animal studies. Seven studies reported beneficial effects or partial protective effects of quercetin on cardiac function in post-ischemic-reperfusion injury and pressure overload animal studies. Meanwhile, the other two studies in pressure overload model reported that quercetin had no effect on cardiac function.
Conclusion: In conclusion, quercetin has the potential ability to improve cardiac function in post-ischemic-reperfusion cardiac injury and pressure overload state.

P26

FRUCTOSE CONSUMPTION AND THE DEVELOPMENT OF METABOLIC SYNDROME IN MALE WISTAR RATS

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Aim: Metabolic syndrome can be classified as group of risk factors that enhances the risk of many health issues particularly diabetes and cardiovascular diseases. The development of metabolic syndrome is mainly contributed by the alteration of dietary intake due to excessive consumption of high fat and carbohydrate diets such as fructose. Thus, this present study aimed to confirm a metabolic syndrome animal model by the induction with fructose drinking water (FDW) in rats.
Methods: 40 male Wistar rats were fed with FDW of 20% for a duration of eight weeks. The physiological variables specifically food, fluid and calorie intake were measured during a period of eight weeks. The metabolic changes with regards to obesity, hyperlipidemia, hypertension and hyperglycemia were determined accordingly.
Results: The consumption of 20% FDW by male Wistar rats for eight weeks led to the development of metabolic syndrome. The intake of 20% FDW significantly ($P>0.05$) elevated the systolic and diastolic blood pressure, blood glucose, triglycerides, total cholesterol, fat mass, percentage mass, body weight, abdominal circumference and BMI of the rats compared to control.
Conclusion: High fructose intake by Wistar rats leads to insulin resistance, hyperinsulinemia, hypertriglyceridemia, and hypertension. This present method of induction offers a more convenient and cost-effective way to induce metabolic syndrome in rats.

P27

PREVENTIVE EFFECTS OF *MORINGA OLEIFERA* ON OBESITY AND HYPERLIPIDEMIA: A SYSTEMATIC REVIEW

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Aim: Obesity and hyperlipidemia are metabolic dysregulation arises from poor lifestyle and excessive dietary intakes. If not treated, it could contribute to many chronic diseases. *Moringa oleifera* (MO) is a plant known to be nutritious. Owing to its medicinal properties, it has been used to alleviate obesity and hyperlipidaemia. This systematic review aimed to investigate the effects of MO on obesity and hyperlipidemia.
Methods: A literature search was done on the effects of MO on obesity and hyperlipidemia using electronic databases which includes Ovid Medline and Scopus. Specific descriptors, i.e. "*Moringa oleifera* OR obesity OR hyperlipidaemia" were used to perform the search. The original articles selected should report the effects of MO on obesity and hyperlipidemia.
Results: 18 articles (8 from Ovid Medline and 10 from Scopus) which complied with the inclusion and exclusion criteria were selected. Based on the chosen articles, MO has the ability to suppress obesity and hyperlipidemia directly and indirectly through the regulation of gene expression, enzyme activity and adipocytokines.
Conclusion: MO demonstrates promising results in alleviating obesity and hyperlipidemia in animal trials. More human trials should be performed on different individuals to strengthen the accomplished effects on animals. Since there were no side effects identified on animal studies, it could be recommended to patients with obesity and hyperlipidemia.

P28

THE EFFECTS OF OIL PALM PHENOLICS (OPP) ON SERUM LIPID PARAMETERS OF GOLDEN SYRIAN HAMSTERS – A PRELIMINARY STUDY

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Aim: The present study was conducted to determine the effects of oil palm phenolics (OPP) on plasma lipid profile of Golden Syrian hamsters. This study presented the preliminary data to explore the potential doses of OPP for the main research in the future.

Methods: Twenty-one male Golden Syrian hamsters were randomly assigned to seven groups: 1) Normal Control (NC); 2) High-Fat High-Cholesterol (HFHC); 3) 0.4mg/kg OPP (0.4-OPP); 4) 0.75mg/kg OPP (0.75-OPP); 5) 1.5mg/kg OPP (1.5-OPP); 6) 3.0mg/kg OPP (1.5-OPP) and 7) 6.0mg/kg OPP (6.0-OPP) treatments. Hamsters in the control group were given normal chow while the rest of the groups were fed with HFHC diet (0.3% cholesterol and 15% coconut oil) for 12 weeks. All the treatment groups were induced with HFHC diet for 4 weeks before proceed with the treatment.

Results: The total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL) and non-high-density lipoprotein (non-HDL) level were significantly increase ($p<0.05$) after 4 weeks of disease induction. A significant reduction of TG ($p<0.05$) level was seen on 0.4-OPP group after 4 weeks of treatment. In addition, a significant reduction was observed on TC, LDL and n-HDL ($p<0.05$) levels of 1.5-OPP group after 8 weeks of treatment.

Conclusion: The present findings show that two doses of OPP, which are 0.4 mg/kg and 1.5 mg/kg, have potential in improving blood lipid profiles in Golden Syrian hamsters and will be used as treatment doses for the main study.

P29

REPEATEDLY HEATED PALM OIL MODULATES CARDIAC GENE EXPRESSION IN SPRAGUE-DAWLEY RATS

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Aims: Oxidisation of cooking oil increases the risk of hypertension by increasing the production of free radicals. The aim of study was to investigate the gene expression profile in cardiac tissue after ingestion of heated palm oil.
Methods: Adult male Sprague-Dawley rats were equally divided into two groups: fresh palm oil and palm oil heated ten times. Blood pressure was measured at the baseline and throughout the 24-week study. At the end of study, the rats were sacrificed. The hearts were isolated for transcriptome analyses.
Results: Repeatedly heated palm oil caused an increase in blood pressure. Microarray analysis identified 219 differentially expressed genes in rats receiving repeatedly heated palm oil compared to the fresh palm oil. The most enriched biological process and molecular function of the significant expressed genes was found to be regulation of response to reactive oxygen species and translational regulator activity, respectively. Pathway analysis showed the significant differentially expressed genes were associated with protein processing in endoplasmic reticulum, protein export and nuclear factor-kappa beta signalling pathways.
Conclusion: Differentially regulated genes involved in the biological pathways provide a molecular explanation for the increased blood pressure. This approach may represent a novel strategy to unravel potentially modifiable pathways and possible therapeutic targets in hypertension.

P30

THE EFFECTS OF ORALLY ADMINISTERED CENTELLA ASIATICA WATER EXTRACT ON SKIN HEALTH: HISTOLOGY ANALYSIS

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Aim: Continuous and prolonged exposure to the ultraviolet (UV) rays of the sun is the major cause of skin damage that leads to photoaging. Oxidative stress has been associated with photoaging. Antioxidants, whether applied topically or consumed orally, have been shown to prevent the UV-induced photodamage. Centella asiatica (CA), locally known in Malaysia as pegaga, contains abundant amount of natural bioactive substances that exhibit antioxidant properties. Previous studies have reported the beneficial effects of this herb in preventing photodamage when applied topically. Because of the high antioxidant content of the herb, the present study aimed to investigate its effects on photodamage upon oral administration of CA using an in vivo animal model exposed to synthetic UV rays.
Method: Groups of female hairless rats were fed with CA water extracts at different concentrations for 10 days. At days 7, 8, 9 and 10, the rats were irradiated with an ultraviolet light machine at the intensity of trice of minimum erythema dose (MED). At day 10, the rats were sacrificed and skin biopsies were taken for histology.
Results: Compared to the control group, rats supplemented with CA showed a thinner epidermis with more rganized collagen fibres and lesser number of sunburn cells. The control group displayed thick keratin that led to epidermal hypoplasia and loss of skin appendages, which are not seen in the treated rats.
Conclusion: Orally administered CA extract protects the skin from the deleterious consequence of UV exposure.

P31

THE EFFECTS OF *CENTELLA ASIATICA* (PEGAGA) ON BODY WEIGHT AND APPETITE

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Aims: *Centella asiatica*, a herbaceous, perennial herb locally known as 'pegaga', is commonly eaten as raw salad in many parts of Asia. Dubbed as one of the 'miracle elixirs in life', *C. asiatica* was reported to have myriads of medicinal properties that include anti-oxidant, anti-inflammatory, antihypertensive, anti-diabetic and anti-anxiety. Previous studies also showed that *C. asiatica* promotes lipolysis in adipocytes. In this study, we investigated the effect this herb has on body weight and appetite in an animal model.
Methods: Five female rats in the treatment group were supplemented with *C. asiatica* water extract at 500 mg/kg body weight for six weeks via oral gavage while four female rats in the control group were given only distilled water.
Results: Compared to the control group, the body weight of rats supplemented with *C. asiatica* extract showed a reduction in body weight. However, the difference was not statistically significant. The supplemented rats had a statistically significant reduction in food intake in the second, fifth and sixth week of treatment duration.
Conclusion: Centella asiatica has an appettite-suppressant effect and may be potentially useful for the treatment and prevention of obesity.

P32

THE USE OF HONEY IN TREATING AND PREVENTING NONSTEROIDAL ANTI-INFLAMMATORY DRUGS-INDUCED GASTRIC ULCER

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Aim: Indigestion and heartburn has been described several centuries ago. Not until the 16th century, gastric ulcer disease was identified. The use of nonsteroidal anti-inflammatory drugs (NSAIDs) is a known cause of gastric ulcer. The use of natural products in treating stomach-related diseases, especially gastric ulcer was actively studied by researchers. This review aimed to evaluate the effectiveness of honey in treating gastric ulcers in animal.
Methods: Original studies on honey as an alternative treatment of gastric ulcer caused by NSAIDs were systematically searched and reviewed. The search only focused on studies using rats model induced by NSAIDs. By using Medline, Scopus and Ebscohost database, potential articles published in English from the year 2000 to 2018 were selected.
Results: The literature search found 30 potential articles but only 5 articles were selected as they met all the inclusion criteria. All selected articles were published between 2001 to 2014. Honey used in the selected articles was from various sources and types with varying doses. All articles reviewed reported the efficacy of honey in treating gastric ulcer through its antioxidant and cytoprotective activities.
Conclusion: Honey is effective in treating gastric ulcer induced by NSAIDs in rat model. However, further studies should be carried out on humans to identify the appropriate doses of honey to maximize its effects.

P33

THE EFFECTIVENESS OF HONEY ON *HELICOBACTER PYLORI* INFECTION: A SYSTEMATIC REVIEW

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Aims: The annihilation of *Helicobacter pylori* (*H. pylori*) is gradually more challenging as resistances to several antibiotics treatment have developed, thus justifying a deeper research on alternative treatment from natural sources. Therefore, this review explores the beneficial effects of honey on *H. pylori*-induced gastric ulcer.
Methods: A systematic research of the effectiveness of honey on *H. pylori* infection using electronic databases including Ovid & Medline, Scopus and EBSCOhost, was performed. The articles from the year 2000 to 2018 reporting the mechanisms and effects of honey on gastric ulcer caused by *H. pylori* infection were assessed and chosen.
Results: A total of 73 articles were identified, and nine articles of honey and its extracts were selected and assessed accordingly in this review. All the studies reported beneficial effects of honey on *H.pylori*-induced gastric ulcer. All selected honey at various concentrations showed inhibition of *H. pylori* with the minimal concentration of 10%. Honey at higher concentrations will achieve the maximal inhibition of nuclear factor-kB (NF-kB) and activator protein 1 (AP-1). Most of the selected honey extracts by diethyl ether solvent produced high inhibition diameters of *H. pylori.*
Conclusion: The findings highlighted the potential of honey in inhibiting the *H. pylori* infection in-vitro. Future extensive studies should be conducted to identify the active components and molecular mechanism of honey on animal and human observational studies to deliver a valid conclusion.

P34

ANTI-ANGIOGENIC POTENTIAL OF *ARDISIA CRISPA* ROOT (MYRSINACEAE) IN RHEUMATOID ARTHRITIS IN VITRO

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Aims: Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory joints disease characterized by excessive angiogenesis. Anti-angiogenesis agent could be a promising therapeutic strategy for RA. *Ardisia crispa* or Mata Itik is a local plant traditionally used for treating various illnesses. Its properties as anti-tumor, anti-inflammatory, and anti-angiogenic have been evidenced in previous studies. However, its role as an anti-angiogenic is yet to be investigated in RA. Thus, the hexane extract (ACRH), quinone rich fraction (QRF), and benzoquinone compound (BQ) isolated from the plant's root were investigated for its anti-angiogenic effect in in vitro angiogenesis assays.
Methods: Cytotoxicity, tube formation, cell invasion, and cell apoptosis assays were performed using HUVEC and HFLS-RA cells.
Results: ACRH, QRF and BQ showed high cytotoxicity against HUVEC (IC_{50} at 1.9 $\pm$ 0.2, 2.5 $\pm$ 0.8 and 1.7 $\pm$ 0.2 g/mL, respectively). Nevertheless, they (ACRH and QRF) were found to be less cytotoxic towards HFLS-RA cell (4.0 $\pm$ 2.3 and 5.7 $\pm$ 0.9 g/mL, respectively) after 24 hours of incubation. Interestingly, BQ still showed higher cytotoxicity towards HFLS-RA cell with IC_{50} at 1.6 $\pm$ 0.5 g/mL. All samples at all concentrations (5, 0.5, and 0.05 µg/mL) significantly inhibited VEGF-induced HUVEC tube formation and IL-1β induced HFLS-RA cell invasion in a concentration-dependent manner. Both ACRH and BQ at highest concentration (5 µg/mL) exhibited late apoptotic activity in IL-1β induced HFLS-RA cell.
Conclusion: This study supported the understanding of the potential of ACRH, QRF, and BQ from *A. crispa* root in suppressing angiogenesis in RA in vitro.

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CURCUMIN MINIMISES HISTOPATHOLOGICAL AND IMMUNOLOGICAL PROGRESSIONS IN COLLAGEN-INDUCED ARTHRITIS IN RATS

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Aims: This study was aimed to investigate the effects of curcumin on histopathological progression and interleukin-1β (IL-1β) levels in collagen-induced arthritis (CIA).
Methods: Thirty male Sprague-Dawley rats (150±50 g) were divided into five random groups. A group was assigned as normal control (CTRL), while the remaining four were subcutaneously immunized with 150 µg collagen emulsion on day-0. CTRL and CIA-Curcumin-d0 groups were supplemented daily with olive oil (1 ml/kg) and curcumin (110 mg/ml/kg) respectively, from day-0. The CIA-OV (negative control), CIA-Beta and CIA-Curcumin-d14 groups were given daily supplementation of olive oil (1 ml/kg), betamethasone (0.5 mg/ml/kg), and curcumin (110 mg/ml/kg) respectively from day 14. The daily oral supplementations were performed for 42 days.
Results: The study showed that groups CIA-Betamethasone ($p=0.00$) and CIA-Curcumin-d0 ($p=0.01$) had significantly lower mean histological scores compared to CIA-OV, respectively. Serum IL-1β levels for CIA-Betamethasone and CIA-Curcumin-d0 were not significantly raised on day 42 compared to day 0. The mean increment of IL-1β levels from day-0 until day 42 were significantly lower ($p\leq0.01$) for all the CIA groups compared to CIA-OV. There were no significant differences in both mean histological score and IL-1β levels of CIA-Curcumin-d0 compared to CIA-Betamethasone.
Conclusion: Early supplementation of curcumin has the potential to minimise disease progression of CIA in rats.

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ANTIPROLIFERATIVE EFFECT OF *Melia azedarach* IN MCF-7 HUMAN BREAST CANCER CELL LINE

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Aims: This study aimed to determine the of antiproliferative effect of seed extract of *Melia azedarach* in human breast cancer (MCF-7) cells.
Methods: This is a quasy experimental study. The human breast cancer (MCF-7) cells were divided into control and three experimental groups. The experimental groups was treated with ethanol extract of *Melia azedarach* at the dose of 40 µg/mL (T1) or 20 µg/mL (T2), or 10 µg/mL (T3). The antiproliferative effects were determined by the percentage of cell accumulation in each phase of cell cycle using PI staining followed by flowcytometry. The data were analyzed using ANOVA test at 95% confidence interval.
Results: The mean percentage of cell accumulation in G0-G1 phase in control group and treated groups were 34.75%, 42.63% (T1), 31.38% (T2), 35.94% (T3) respectively. The percentage of cell accumulation in G0-G1 was higher in T1 group than those of control, T2 and T3 groups ($p<0.05$). The mean percentage of cell accumulation in S phase in control group and treated groups were 21.41%, 21.24% (T1), 21.31% (T2), 20.74% (T3) respectively. The mean percentage of cell accumulation in G2-M phase in control group and treated groups were 26.86%, 24.84% (T1), 19.80% (T2), 25.95% (T3) respectively.
Conclusion: The ethanolic extract of Melia azedarach seeds shows antiproliferative effect on MCF7 Human breast cancer cell by increasing the percentage of cell accumulation in G0-G1 phase.

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THE EFFECT OF *Typhonium flagelliforme* ETHANOLIC EXTRACT ON IMMUNE SYSTEM IN C3H MICE WITH MAMMARY ADENOCARCINOMA

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Aims: This study aimed to investigate the effect of T*yphonium flagelliforme* ethanolic extract on immune system in C3H mice with mammary adenocarcinoma.
Methods: This was an experimental study with pre and post test design. A total of 12 male C3H mice were inoculated with mammary adenocarcinoma. The effect of *Typhonium flagelliforme* ethanolic extract on immune system were evaluated based on the level of interferon gamma (IFN-γ), tumour necrosis factor-alpha (TNF-α), and the expression of vascular endothelial growth factor (VEGF) and Ki67. The significant difference between pre and post treatment was analyze using T-dependent test with level of significant at 0.05.
Results: There was an increase in IFN-γ level in rats after being treated with ethanol extract of *Typhonium flagelliforme* compared to before treatment ($p<0.05$). However, there was no significant difference between TNF-α level in rats after being treated with ethanol extract of *Typhonium flagelliforme* compared to before treatment. The increase in IFN-γ level after treated with ethanol extract of *Typhonium flagelliforme* might lead to apoptosis via increasing caspase 3 expression ($p<0.05$) and decreasing VEGF expression ($p<0.05$) and ki67 expression ($p<0.05$).
Conclusion: *Typhonium flagelliforme* could increase IFN-γ level and the expression of caspase 3 along with a decrease in the VEGF and Ki67 expression in C3H mice with mammary adenocarsinoma.

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COMPARISON BETWEEN *HOLOTHURIA EDULIS* (SEA CUCUMBER EXTRACT) AND *LABISIA PUMILA* (ALCOHOL EXTRACT) ON WOUND HEALING PROCESS IN ANIMAL MODELS

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Aims: *Holothuria edulis* and *Labisia pumila* are widely recognized to South East Asia natives as traditional medicine for generations. The former is a type of pinkish black sea cucumber which is commonly used to heal superficial wound, whereas the latter is a herb named "Kacip Fatimah" that has been used exclusively in post-menopausal and post-partum medication. In Malaysia, there are eight variants of *L.pumila* and among those, var.*pumila* and var.**alata** are the most ubiquitous and researched.

Methods: *H.edulis* were extracted using phosphate buffer solution (PBS) while leaves and roots of *L.pumila* were alcohol-extracted. Male Sprague-Dawley rats (n=72) weighed between 250-300 gram were divided into 8 groups with 9 rats each: Normal group, positive control (acriflavin), negative control (ointment), *H.edulis*, var.*pumila* (leaves), var.*pumila* (roots), var.*alata* (leaves), and var.*alata* (roots). Four wounds of 6 mm in diameter were inflicted on dorsal surface of rats with disposable punch biopsy. Wounds were treated daily accordingly and wound contraction was measured using a digital caliper until fully closed.

Results: Average wound healing day analysis demonstrated that var.*pumila* leaves had significant and the fastest healing compared to normal, positive control, negative control, and *H.edulis* groups ($p<0.05$).

Conclusion: *L.pumila* var.*pumila* (leaves) extract significantly expedites the wound healing process and is significantly better than sea cucumber.

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MALAYSIAN PROPOLIS AND METFORMIN MODULATE OXIDATIVE STRESS BY UP-REGULATING NRF2 IN DIABETIC RAT TESTIS

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Aim: Testicular oxidative stress has been reported to be the main cause of reproductive impairment in male diabetics. Therefore, we examined the effects of Malaysian propolis (MP), metformin (Met) and their combination, on testicular oxidative stress in diabetic state.
Methods: Thirty adult male Sprague-Dawley rats were randomly divided into 5 groups (n=6). The rats were either treated with distilled water [normal control (NC) and diabetic control (DC)], MP [diabetic+MP (300 mg/kg b.w./day)], Met [diabetic+Met (300 mg/kg b.w./day)] or MP and Met (diabetic+MP+Met), for four weeks. Diabetes was induced by a single intraperitoneal injection of streptozotocin (60 mg/kg b.w.).
Results: We observed significant decreases in mRNA transcript levels of nuclear factor erythroid 2-related factor 2 (Nrf2) ($p<0.05$), superoxide dismutase (SOD) ($p<0.001$) and catalase (CAT) ($p<0.001$) and a marginal decrease in glutathione peroxidase (GPx) in the testis of DC group, compared to NC group. Also, the activities of SOD, CAT, GPx, glutathione-S-transferase and glutathione reductase decreased significantly ($p<0.001$), total glutathione level and total antioxidant capacity (TAC) decreased significantly ($p<0.001$), while nitric oxide (NO) and malondialdehyde (MDA) levels increased significantly ($p<0.001$) in the testis of DC group, relative to NC. Treatment with MP, Met or their combination, significantly up-regulated Nrf2, SOD, CAT and GPx mRNA transcript levels, and increased antioxidant enzymes activities and TAC, decreased NO and MDA levels, with the combined intervention showing the best results.
Conclusion: Malaysian propolis ameliorates DM-induced testicular oxidative stress by up-regulating Nrf2, and exerts better beneficial effects when combined with metformin.

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RECOVERY EFFECTS OF *EURYCOMA LONGIFOLIA* STANDARDIZED EXTRACT ON RATS WITH POLYCYSTIC OVARIAN SYNDROME

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Aim: Polycystic ovarian syndrome (PCOS) is characterized by cystic follicles in the ovary, hyperandrogenism and anovulation. Plants have long been used traditionally to treat diseases as they are believed to be less harmful than conventional drugs. *Eurycoma longifolia* is a plant native to Malaysia and it is recognized for its effects on males. However, its function in women is unclear justifying its exposure to experimentally-induced PCOS in female rats in this study.
Methods: PCOS was induced with a single subcutaneous injection of estradiol valerate (EV) (2 mg/rat). At the end of 60 days, rats were then treated with *E. longifolia* standardized extract and clomiphene citrate for 28 consecutive days. Oestrous cycle was monitored daily during induction and treatment periods. Rats were sacrificed at day 28 and blood samples were drawn for serum oestradiol, testosterone, progesterone, LH and FSH analyses. Ovaries were collected for histology and immunochemical staining and steroidogenic genes expression was evaluated by quantitative RT-PCR.
Results: Disruption of oestrous cycle with the presence of cystic follicles and absence of corpora lutea were apparent in the ovary of EV-induced rats while oestrous cycle and hormonal imbalances were restored with improvement in the histology of the ovary in *E. longifolia* treated rats.
Conclusion: *E. longifolia* at 100 mg/kg has the potential to restore oestrous cycle and improve the morphology and histology of EV-induced ovary by maintaining hormonal balances and steroidogenesis. The potential effects of the extract may be explored further for the management of PCOS and female disorders.

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GLUT-4 IMPROVEMENT IN RATS AFTER PORANG (*AMORPHOPHALLUS MUELLERI* BLUME) GLUCOMANNAN SUPPLEMENTATION

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Aims: Insulin resistance (IR) is considered as a key component in the development of metabolic syndrome (MetS). Dietary fiber can control body weight, insulin sensitivity, and thus manage the risk factors of MetS. Glucomannan Porang (GMP) is a dietary fibre derived from porang (*Amorphophallus muelleri* Blume), an indigenous Indonesian plant. This study aimed to investigate GLUT-4 level after GMP administration in MetS induced rats.
Methods: Randomized post-test only control group design was applied to this study. A total of thirty Sprague Dawley rats was divided into 5 groups: Normal, MetS, GMP25, GMP50, and GMP100. Normal group only received AIN-93M, while other groups were fed with high fat & fructose (HFHF) diet as an inducer of MetS for 21 days. After 21 days induction, 25 mg/kg BW GMP, 50 mg/kg BW GMP, and 100 mg/kg BW GMP were given at the last 28 days to rats in the respective groups. Serum was collected on day 49, GLUT-4 was measured using ELISA. Data was analyzed using ANOVA followed by LSD post hoc test ($p<0.05$).
Results: GMP supplementation improved GLUT-4, the insulin resistance marker. The highest GLUT-4 level (12.85$\pm$01 ng/mL) was found in GMP100 group, on par with the level of normal group (12.87$\pm$0.2 ng/mL). For GMP50 (10.33$\pm$0.1 ng/mL) and GMP25 (9.08$\pm$0.6 ng/mL) groups, the GLUT-4 level was higher than the level of MetS (7.29$\pm$0.14 ng/mL).
Conclusion: Glucomannan Porang (*Amorphophallus muelleri* Blume) supplementation can improve GLUT-4 level in rats with MetS.

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STAMINA ENHANCER HERBS ADDED TO THE *FORMULA JAMU ANTIHIPERTENSI* REDUCES ITS ANTIHYPERTENSIVE EFFECT

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Aims: *Formula Jamu Antihipertensi* (FJA) is a jamu consisting of three blood pressure-reducing herbs, i.e. the extract of celery, cat's whiskers and Asiatic pennywort. The *Formula Jamu Antihipertensi* Plus (FJA-Plus) is a jamu consisting of three blood pressure-reducing herbs previously mentioned, plus three herbs for stamina enhancer, i.e. the extract of *Phyllanthus niruri* L., *Curcuma xanthorrhiza* Roxb. and turmeric. This study aimed to compare the effectiveness of antihypertensive effect between FJA and FJA-Plus.

Methods: The pretest-posttest control group study was conducted on Wistar hypertensive rats divided into 3 groups randomly. Group 1 and 2 were treated with a single dose of FJA and FJA-Plus respectively, each with a dose of 18 mg/kgBW and 72 mg/kgBW. While Group 3 was treated with a single dose of 3mg/kgBW of captopril as a control. The systolic and diastolic blood pressure were measured at 1 and 2 hours post treatment. The data obtained were analyzed using dependent t-test, independent t-test, and one- way analysis of variance at the level of significance of $p<0.05$.

Results: The treatment with FJA and FJA-Plus could reduce the blood pressure more effective than captopril. Treatment with FJA decreased the blood pressure greater than FJA-Plus ($p<0.05$).

Conclusion: The three stamina-enhancing herbs added to FJA-Plus decrease the antihypertensive effects of FJA in hypertensive rats.

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Antihypertensive Activities of Standardised *Moringa Oleifera* Lam (Merunggai) Extracts in Spontaneously Hypertensive Rats

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Background: *Moringa Oleifera* (Moringaceae), an edible plant indigenous to India and can be found in tropical and subtropical areas. Fruits and leaves of this plant are used in cooking due to its high in nutritional values. Various plant parts also have been used traditionally as cardiac tonic and diuretic. In recent years, *M. Oleifera* has received a commercial interest for maintaining good health and lowering blood pressure.
Methods: The ethanolic extracts and aqueous extracts were fed to rats once daily for 14 days. Systolic and diastolic blood pressure (BP) of rats were measured on day 1 and day 15. Urine of these rats were collected on day 14 and the volumes were measured. Angiotensin converting enzyme (ACE) inhibitory activity of the extracts was also investigated.
Results: On day 15, except for the aqueous stem extract (AEE), all other extracts showed a significant reduction of systolic and diastolic BP in spontaneously hypertensive rats (SHR) when compared with the negative control but none of the extracts had significant hypotensive effect on normotensive (NT) rats. Ethanolic leaf extract (ELE) caused diuresis significantly when compared with the negative control. Moreover, most of the extracts inhibited ACE activity significantly at 40 µg/ mL and 80 µg/ mL when compared with the negative control. ELE, aqueous leaf extract (ALE) and ethanolic pod extract (EPE) showed the highest levels of inhibition (>50%) and their IC_{50} values were determined.
Conclusion: The active extracts are worthy of further investigation as they have the potential to be developed as dietary supplements for pre-hypertensive individuals.

Keywords: *M. Oleifera*, systolic blood pressure, diastolic blood pressure, diuretic, ACE inhibition

Unmet Need for Family Planning among Reproductive Age Women with Heart Disease in Malacca

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Background: Majority of all pregnancy-related deaths are avoidable if all women have access to effective reproductive health care services since non-use of contraception cause serious health consequences of unintended and high risk pregnancies. Unmet need for family planning is a public health problem for maternal health especially for women with known heart disease which resulted in higher rates of maternal morbidity and mortality. The need of women with heart disease toward use of family planning should be addressed and factors contribute to family planning use should be explored. The objective of this study is to determine the prevalence and factors of unmet need for family planning among reproductive age women with heart disease

Methods: A cross sectional study was conducted in Malacca Hospital from 1st Januari 2015 hingga 31st Disember 2015 among women aged 15-49 years old diagnosed with heart disease using face-to-face interviews

Results: Multivariate Logistic Regression analysis show predictors for non use of family planning are younger age, infrequent follow up with specialists, history of comorbidity, history of prematurity and history of hypertension in pregnancy

Conclusion: Pre-pregnancy counselling plays an important role to address reproductive need among women with heart disease who are susceptible toward high risk pregnancy and to further reduce level of unmet need for family planning among these women. This should involve providing wide choice to these women for fertility regulation and ensuring safe pregnancy and delivery.

Keywords: Women, reproductive age, heart disease, family planning, unmet need

Biosynthesized Gold Nanoparticles Using *Lignosus Rhinocerotis* and Chitosan as a Healing Accelerator for Diabetic Wound

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Background: Management on diabetic wounds by offering correction of biological abnormalities caused by hyperglycaemia and prevention of infection is currently not available. This could be attained by applying an approach that combining inhibition of prostaglandin transporter (PGT) which will promote wound healing using Dicer subtract small interfering RNA (DsiRNA) and gold nanoparticles (AuNPs) with antibacterial properties.
Methods: AuNPs were produced via green synthesis using different concentrations of cold and hot sclerotium of *Lignosus rhinocerotis* extract (CLRE and HLRE, respectively), a type of mushroom, also known as Tiger Milk Mushroom. Chitosan (CS) was added into the formulation as stabilizer to prevent particle aggregation.
Results: Chitosan stabilized AuNPs (CS-AuNPs) exhibited surface Plasmon resonance (SPR) band at a wavelength of 533 nm as determined by UV-vis spectrometer. Particle size of CS-AuNPs synthesized using CLRE and HLRE formed an average particle size in the range of 202 $\pm$ 49 to 273 $\pm$ 79 nm and 190 $\pm$ 31 to 322 $\pm$ 28 nm, respectively. FTIR spectra suggested the involvement of protein and polysaccharides in CLRE and HLRE as reducing biomolecules, reducing gold ions into AuNPs. CS-AuNPs formed were spherical, triangular, pentagonal and irregular in shape. X-Ray Diffraction analysis confirmed that CS-AuNPs synthesized using HLRE had a better crystallinity compared to CLRE. CS-AuNPs synthesized by both types of extracts displayed effective antibacterial activity against Gram-negative bacteria (*Pseudomonas aeruginosa* and *Escherichia coli*) and Gram-positive bacteria (*Staphylococcus aureus*).
Conclusion: The multi-actions of these nanocomposites are expected to be useful as healing promoter for diabetic wound treatment.

Keywords: Green Synthesis, Tiger Milk Mushroom, metal nanoparticles, antibacterial agent, Diabetes mellitus

Screening Apnea on the Move: A Computational Study of Onset in Soft Palate Snoring with Varying Airway Obstruction

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Background: Obstructive sleep apnea (OSA) is a serious disorder associated with repeated obstruction (either partial or complete) of the airway during sleep. Severe degrees of apnea affects the quality of sleep and oxygen saturation during sleep, leading to daytime fatigue and has been linked to hypertension and cardiac problems. Studies have suggested that OSA is perhaps more common than originally perceived, but present diagnosis of OSA that involves sleep tests are not practical for screening of OSA in the mass population. The present study aims to explore alternative means for screening OSA from snoring signals by investigating the effect of varying airway obstruction on the onset for soft palate snoring.
Methods: We adopt a computational fluid-structure interaction study to investigate flutter of the soft palate under varying degree of airway obstruction. To that end, the airway is idealised as a 2-D channel with localised blockage and the soft palate is represented as a cantilever plate. Cantilever plate properties were set to vibrate within typical soft palate snoring frequencies. Critical flow velocity for cantilever plate flutter was determined for different depths of channel blockage.
Results: Critical flow velocity for flutter of cantilever plate decreased with increasing depth of localised channel blockage. This implies that soft palate snoring may begin at lower flow velocity with increasing airway obstruction.
Conclusion: As flow velocity varies periodically during a breathing cycle, patients with airway obstruction is anticipated to show earlier onset of soft palate snoring. Therefore, time for onset of palatal snoring may be analysed as a marker to estimate degree of airway obstruction and further developed for potential mass screening of OSA.

Keywords: Obstructive sleep apnea, flutter, palatal snoring, flow-induced vibration, snoring acoustics

QRS Onset Detection of ECG Signal using Secant Line Slope Method

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Background: In automatic electrocardiographic signal analysis, the beginning of Q-wave or QRS onset must be identified prior to QT interval or QRS duration measurements. These measurements are decisive ECG parameters for diagnosing cardiac abnormalities among cardiologists. Hence, the efficiency of the developed automatic algorithm to identify the QRS onset is essential to obtain an accurate result of the ECG parameters.
Methods: In this report, an algorithm to identify the QRS onset based on secant line slope formula is proposed. The preprocessing and wave delineation process were implemented in MATLAB using modified Pan-Thompkins algorithm (an established adaptive threshold method). The window of the preceding Q-wave was determined before calculating the slope of secant line along the descending slope for QRS onset identification. The performance of the proposed algorithm was evaluated using 25 subjects from PPUKM (Pusat Perubatan Universiti Kebangsaan Malaysia) and volunteered participants under the approval of Research and Ethics Committee, PPUKM (Code of ethics approval: FF-2013-313). All data were acquired using biosignal amplifier (g.USBamp by g.tec, Austria) with 2 minutes duration of recording and sampled at 512 Hz.
Results: The efficiency of the proposed algorithm has obtained a sensitivity of 99.67%, and accuracy of 99.07%.
Conclusion: The result shows stable performance and insensitivity of the proposed algorithm towards ECG wave morphology changes. The completion of the algorithm for automatic measurement of ECG parameters will depend on combining the QRS onset algorithm with the upcoming detection algorithm (QRS offset or T-wave offset). The complete algorithm can be used as the basis of software development in the future.

Keywords: Automated ECG algorithm, QRS onset, secant line slope

The Role of Annatto Tocotrienol in Preventing Cartilage and Subchondral Changes in a Rat model of Osteoarthritis

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Background: Osteoarthritis is a localized inflammatory disease of the joint affecting both the cartilage and subchondral bone. Supplementation of anti-inflammatory compounds like tocotrienol could prevent joint degeneration. The objective of this study was to determine the effects of oral annatto tocotrienol supplementation in preventing the deterioration of cartilage and subchondral bone in a rat model of osteoarthritis induced by monosodium iodoacetate (MIA).
Methods: Three-month-old male Sprague-Dawley rats (n=30) were randomized into five groups (n=6/group). Osteoarthritis was induced in four of the groups with a single injection of MIA at week 0. The normal control group was injected with equivolume of normal saline. Three osteoarthritic groups were supplemented with annatto tocotrienol at 50, 100 and 150 mg/kg/day orally for five weeks. The normal and negative controls were supplemented with equivolume of olive oil. All rats were sacrificed at week 5, and the blood and tibial-femoral joints were collected for analysis.
Results: Monosodium iodoacetate caused significant deterioration of the cartilage and erosion of the subchondral bone. Annatto tocotrienol at 100 and 150 mg/kg/day ameliorated the adverse effects of MIA as indicated by the lower histological scores of the joint and cartilage remodelling markers. Annatto tocotrienol at 150 mg/kg/day also reduced the osteoclast surface of the subchondral bone and bone remodelling indicated by osteocalcin level.
Conclusion: Annatto tocotrienol at 100-150 mg/kg/day can prevent degenerative changes of the cartilage and subchondral bone compartments of the joint in rats with osteoarthritis. Its joint-sparing mechanism should be evaluated in future studies.

Keywords: Articular cartilage, inflammation, knee, joint, vitamin E

Biosynthesized Silver and Gold Nanoparticles as Potential Antibacterial Agents for Wound Dressing

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Background: Silver and gold nanoparticles (AgNPs and AuNPs, respectively) have been developed as alternative antimicrobial agents due to the increase of antibiotic resistance traits in bacteria. The green synthesis of AgNPs and AuNPs will ensure a simple, cost effective and environmentally friendly method is used. The objective of this study was to biosynthesize AgNPs and AuNPs using *Pleurotus ostreatus* (oyster mushroom) spent mushroom substrate (SMS) as antibacterial agent for chronic wounds. SMS is the residual material remaining after a harvest of mushrooms which contains proteins, amino acids and enzymes, a new source of reducing agents.
Methods: In this study, biosynthesized AgNPs and AuNPs were produced using different concentrations of aqueous extract SMS and later, stabilized using chitosan, a cationic polysaccharide. The formation of nanoparticles were determined using UV-vis spectrometer and FTIR while their particle size and morphology were analyzed using dynamic light scattering method and transmission electron microscopy, respectively. Their antibacterial activity was also determined using microdilution method against selected bacteria strains.
Results: The peak was observed at 420 to 490 nm and 520 to 550 nm corresponding to the Plasmon absorbance of AgNPs and AuNPs, respectively, as determined by UV-vis spectrometer, indicating the formation of the respective nanoparticles. FTIR analysis confirmed the role of SMS as reducing and capping agent of Ag^+ and Au^+ ions to AgNPs and AuNPs, respectively. TEM showed that the formed nanoparticles were spherical in shape with the size in the range of 30.10-3.45 nm and 23.85-5.72 nm for AgNPs and AuNPs, respectively. These nanoparticles exhibited effective antibacterial activity against Gram positive bacteria *(S. aureus and Bacillus)* and Gram negative bacteria *(E. coli and P. aeruginosa).*
Conclusion: These nanoparticles exhibited antibacterial activity that promises potential use in wound dressing for treating chronic wounds.

Keywords: Chitosan, Green synthesis, Oyster mushroom, metal nanoparticles

Development of Health Monitoring System for IoT with MySignals and LoRa

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Background: Internet of Things (IoT) is a fast-growing worldwide network of interconnected variety of objects that supports many input-output devices, sensors and actuators based on standard communication protocol. IoT based health monitoring system is now in the top peak because of its potentialities among all other IoT applications. Wearable sensors integrated with IoT healthcare can effectively analyse and gather the patients' physical health data that has made the IoT healthcare ubiquitously acceptable. A set of challenges including the continuous presence of the healthcare professionals and the proper amenities in remote areas during emergency situations need to be addressed for developing a flexible IoT based health monitoring system. Besides, the human entered data is not as much reliable as automated generated data. Development of IoT based health monitoring system allows a personalized treatment in certain circumstances that helps to reduce the healthcare cost and wastage with a continuous improving outcomes.
Methods: We present an IoT based health monitoring system using the MySignals development shield for Arduino Uno. MySignals enables multiple wearable sensors to gather the physical data. The aim is to transmit the gathered data from MySignals to a Cloud server or Personal Computer by implementing a wireless system with LoRa.
Results: The results show that MySignals is successfully interfaced with the ECG, temperature, oxygen saturation and pulse rate sensors. The communication with the hyper-terminal program using LoRa has been implemented and an IoT based health monitoring system is being developed in MySignals platform with the expected results getting from the sensors.
Conclusion: The paper represents the development of an IoT based health monitoring system that focuses on the wearable sensors connected to the MySignals platform and LoRa. LoRa and MySignals platform have several promising characteristics that is capable of taking part in a successful development of IoT based health monitoring system.

Keywords: IoT based healthcare, Wearable sensors, MySignals platform, LoRa

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Bone Health Status of Malaysia Middle-Aged and Elderly Populations

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Background: Osteoporosis is a growing health problem in Asian countries with a rapidly expanding ageing population. However, there is a paucity of data on the bone health status of Malaysian middle-aged and elderly population. This study aimed to determine the prevalence of osteoporosis among populations aged ≥40 years in Klang Valley, Malaysia.
Methods: A cross-sectional study was conducted from April 2018 to September 2018, involving 324 respondents (111 men, 213 women) aged ≥40 years in Klang Valley, Malaysia. Information on subjects' demography, medical history, lifestyle, and physical activity status was obtained. The body anthropometry of the subjects was also measured. They underwent a bone mineral density scan (hip and lumbar spine) using a dual- energy X-ray absorptiometry device. Differences in the proportion of subjects in each bone health category (normal, osteopenia or osteoporosis) according to demography, diet habits and lifestyle practices were analysed using chi-square test.
Results: The prevalence of osteoporosis was 9.9% in men and 18.3% in women ($p<0.05$). The prevalence of osteopenia and osteoporosis was significantly increased in women with higher age ($p<0.05$). Ethnic differences in the prevalence of bone health was observed ($p<0.001$). The prevalence of osteoporosis was significantly higher among menopausal women ($p<0.001$). The prevalence of osteopenia/ osteoporosis was significantly higher among underweight subjects ($p<0.001$). There was no association between other demographic details and the prevalence of suboptimal bone health among subjects ($p>0.05$).
Conclusion: Suboptimal bone health among middle-aged and elderly Malaysians are associated with sex, increased age, ethnicity, menopause and being underweight. This study highlights the need for osteoporosis prevention strategies among elderly and postmenopausal women.

Keywords: Aging, menopause, bone density, osteopenia, osteoporosis

Osteoporosis among Middle-aged and Elderly Population in Klang Valley, Malaysia: Knowledge, Belief and Practices

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Background: Osteoporosis is a growing health problem around the world. A good knowledge and awareness of the disease are pre-requisites for success in preventive measures and modifications in lifestyle. Hence, this study investigate osteoporosis knowledge, beliefs and bone health practices among Malaysians aged 40 years and above.

Methods: A cross-sectional study was conducted among 324 respondents (111 males, 213 females) aged 40 years and above who were recruited from Universiti Kebangsaan Malaysia Medical Centre (UKMMC) and Klang Valley area. Self-administered questionnaire was used consisting of osteoporosis knowledge, belief and practices regarding smoking behaviour, dairy intake, coffee or tea drinking habits and physical activity.

Results: The mean age of the subjects was 57.31 $\pm$ 9.20 years. The findings indicated high level of knowledge and health beliefs regarding osteoporosis with mean score of 8.09 $\pm$ 1.51 and 42.79 $\pm$ 3.38, respectively. Osteoporosis knowledge varied significantly with sex and education level ($p<0.05$). Furthermore, health belief was significantly different in relation to age groups, ethnicity and education level ($p<0.05$). Moderate dietary and lifestyles practices were indicated, a significant relationship was found between dairy intake and ethnicity ($p<0.05$), smoking status among sex and ethnicity ($p<0.05$). Knowledge showed a significant positive relationship with health belief ($r= 0.235$, $p<0.001$) and with coffee or tea intake ($r= 0.148$, $p=0.008$). While negative relationship was found between knowledge and smoking status ($r= -0.128$, $p=0.021$). Osteoporosis health belief was significantly correlated with dairy intake ($r=0.199$, $p<0.001$) and physical activity ($r=0.176$, $p=0.001$). Negative correlation was noted between health belief and smoking status ($r=-0.112$, $p=0.043$).

Conclusion: Knowledge played a significant role in affecting health belief and osteoprotective practices towards osteoporosis. Determination of bone health status

may be needed to assess whether good knowledge, health belief and practices regarding osteoporosis translated into better bone health.

Keywords: Attitude, perception, dietary habits, lifestyle practices, bone health

Graphene Oxide and Reduced Graphene Oxide Hydrogels as Antibiofilm Wound Dressing for Wound Infection

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Background: Biofilm is bacteria attached to wound surfaces and is a major contributor to non- healing wounds. It is found that the increased resistance of biofilms to antibiotics allows wound infections to persist chronically in spite of antibiotic therapy. In this study, GO and rGO were explored as a plausible antibiofilm agents.
Methods: The rGO was synthesized via reducing the functional groups of GO. Then, GO and rGO were characterized using zetasizer, X-ray photoelectron spectroscopy, UV-Vis spectroscopy and FESEM. The GO and rGO were then formulated into hydrogels and tested for antibiofilm activities in vitro using XTT test, and in vivo biofilm formation assay using nematodes *C. elegans*.
Results: As a result, rGO was successfully formed with a reduction of functional groups up to 95%. The conversion was confirmed by UV-Vis and FESEM. Sonication time of 120 minutes reduces particle size of GO and rGO to 248.7 $\pm$ 2.0 and 372.8 $\pm$ 2.3 nm respectively. The rGO hydrogels showed significant reduction of biofilm formation in *S. aureus* (81-84%) and *P. aeruginosa* (50-62%). The fluorescence intensity also confirmed that rGO can inhibit biofilm bacteria in *C. elegans* experiment.
Conclusion: This study implied that rGO hydrogel is an effective antibiofilm agent for infected wounds.

Keywords: Graphene oxide, reduced graphene oxide, antibacterial, antibiofilm, chronic wound healing

Titanium/Wollastonite Composite: A Candidate for Bone Implant Materials Prepared by Powder Injection Molding

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Background: Ti6Al4V alloy has been successfully used widely in implants due to high chemical stability, mechanical properties and biocompatibility. Wollastonite (WA) is bioactive materials which can react with the surrounding tissue by promoting rapid fixation and bonding between bone and implant materials. Ti6Al4V cannot form chemical bonding with human bone while WA can actively promote new bone formation. By combining both materials, Ti6Al4V/WA composite can become excellent in mechanical properties also in bioactivity. PIM is one of capable process to produce intricate geometric parts in large, cost effective which difficult to achieved with other manufacturing process.
Methods: 90 wt.% of Ti6Al4V and 10 wt.% Wollastonite were mixed together with 60 wt.% palm stearin and 40 wt.% polyethylene as binder to get a homogenous feedstock. The feedstock was injected into mould in tensile bar shaped. The feedstock was debound using solvent and thermal debinding stage to eliminate binder system. Then, the sample were sintered at 1300˚C. Physical and mechanical were analysed on sintered sample as well as biocompatibility test using PrestoBlue™ reagent.
Results: The homogenous feedstock was successfully made and injected with no defects. Young's modulus of sintered Ti6Al4V/WA are in the range of human bone strength with 18.10 GPa. Biocompatibility test shows that absorbance increased with days indicates the growth of cells and non-toxic.
Conclusion: Ti6Al4V/WA composite can be manufactured successfully using PIM method with no defects. Biocompatibility test shows the composite is non-toxic and can be used in bone implant applications.

Keywords: Titanium-wollastonite composite, powder injection molding, physical properties, mechanical properties, biocompatibility

Predictors of Bone Health among Malaysians Aged 40 Years and Above in Klang Valley

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Background: The prevalence of osteoporosis in Malaysia is escalating with the expanding ageing population in Malaysia. Information pertaining to the risk factors of osteoporosis is important to strategize prevention effort in this country. This study aimed to identify the predictors of osteoporosis among Malaysians aged ≥40 years in Klang Valley.
Methods: A cross-sectional study was conducted among 324 subjects aged ≥40 years in Klang Valley, Malaysia. All subjects completed a structured questionnaire comprising of demographic details, lifestyle, physical activity status and medical history. Their bone health status was measured using a dual-energy X-ray absorptiometry device. The association between risk factors and bone health status (normal/suboptimal bone health) was assessed using logistic regression analysis.
Results: The study showed that 61.4% subjects had suboptimal bone health (osteopenia/osteoporosis). Sex, ethnic, body weight and fat mass were the significant predictors of bone health among the subjects. Females have 4.09 times the odds of suffering from suboptimal bone health compared to males *(95% CI 1.20, 14.00)*. The Indian population had 0.12 times the odds of suffering from suboptimal bone health than the Chinese population *(95% CI 0.04, 0.35)*. Sub-analysis based on sex showed that menopausal women had 4.61 and 2.97 times the odds of suffering from suboptimal bone health compared to pre-menopausal women *(95% CI 1.81, 11.76)* and peri-menopausal women *(95% CI 1.03, 8.55)*, respectively.
Conclusion: Suboptimal bone health is associated with sex, ethnic, body weight and fat mass among Malaysians aged ≥40 years. Among women, suboptimal bone health was predicted by their menstrual status. Proper measures must be taken to reduce the progression of osteoporosis among high-risk individuals.

Keywords: Asian, bone density, menopause, osteopenia, osteoporosis

The Development and Characterization of Moringa Oleifera Aqueous Leaf Extract Loaded Phospholipid Complexes for Wound Healing Application.

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Background: The aqueous leaf extract of Moringa Oleifera has showed marked wound healing activity in various studies. Nevertheless, exploration of the potential utility of the extract into a wound healing formulation is limited. This study aims to formulate phospholipid complexes containing Moringa Oleifera aqueous leaf extract and examine its prospective to be used as wound healing aid.
Methods: Extraction of the Moringa Oleifera leaves was carried out through maceration and the bioactive constituents in the extract was identified using LCMS. Phospholipid complexes containing MO (MOPCT) was formulated and characterised for their particle size, polydispersity index, zeta potential, morphology and encapsulation efficiency. Cell viability assay was done to investigate the potential toxicity of the MOPCT to normal human dermal fibroblast cells (NHDF). Cell migration assay was done to study the effect of the MOPCT on cell migration and proliferation.
Results: Bioactive vicenin-2 and other compounds were detected in the extracts. The MOPCT remain stable up to 25 days in 4°C in terms of particle size and zeta potential. The phospholipid complexes morphology appeared in the form of multilamellar vesicles under TEM. However, the encapsulation efficiency of vicenin-2 in the phospholipid complexes is poor (<1%). MOPCT(F) showed the highest NHDF migration and proliferation rate in comparison to the extract and other formulations.
Conclusion: MOPCT has shown wound healing properties in comparison to the extract itself. The formulation may be further studied in order to identify the bioactive compound that is responsible for wound healing activity of the extract, further optimised and developed into wound dressing preparation.

Keywords: *Moringa Oleifera*, leaf extract, phospholipid complexes, wound healing

Relaxation Effect of *Hippobroma Longiflora* Alkaloids on Rat Isolated Rat Tracheal Rings.

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Background: *Hippobroma longiflora (L) G. Don* is a perennial herbaceous species, harvested for local medicinal uses and also an ornamental plant. The phytochemical investigations on the whole plant of *Hippobroma longiflora* have resulted in the isolation and elucidation of new diphenethylpiperidine alkaloid, namely hippofoline B (1), alongside two known alkaloids, namely, (-)-lobeline (2) and (-)-*cis*-2',2'-diphenyllobelidiol (3). The alkaloid lobeline, is well known for its beneficial effects on the function of the respiratory tract including stimulating breathing, supporting the cough reflex and also shown to reduce vascular tone. The main aim of this study was to investigate the pharmacological effects of compound 1-3 on rat isolated tracheal rings.

Methods: Using the standard organ bath procedures, the tracheal rings were obtained from 6 to 8 week-old male Sprague Dawley rats (UNMC12).

Results: All the compounds studied showed a significant relaxation effect against carbachol- induced contraction (1 μM), with maximal responses (E_{max}) of, 110.1 ± 9.0%, (1) (n=6), 121.0 ± 3.3%, (2) (n=5), and 115.6 ± 3.4 %,(3) (n=7), when compared to control (44.0 ± 5.8 %, n=8). The present study indicated that all the compounds tested have a higher relaxation effect when compared to atropine (102.1 ± 5.8 %, n=8).

Conclusion: From these observations, compounds 1-3 improved the potency of tracheal segments. However, its precise mechanism of action has yet to be elucidated.

Keywords: *Hippobroma Longiflora,* alkaloids, organ bath, relaxation, and trachea

Physical Inactivity and Motivation: A Cross Sectional Study

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Background: Physical inactivity ranked the fourth leading risk factor for global mortality and an alarming estimation of 3.2 million deaths globally as its results (WHO 2017). Malaysia has been recognized one of the least physically active countries in the world with more than 60% of adults being essentially sedentary (Boon et al 2016). One of the best ways to encourage an individual to engage in physically active is to determine their motivation for participating in Physical Activity (PA). This study aimed to find out the motivation towards the engagement of PA among Malaysian adults.
Methods: A total of 309 participants aged 18 to 64-year-old were included from Gombak district, Malaysia in this cross sectional study. Each participants provided consent form, demographic, The Physical Activity and Leisure Motivation Scale (PALMS).
Results: The difference in active level of PA among the BMI groups of underweight (48.6%), normal (50.3%), overweight (63.4%) and obese (42.2%) were not statistically significant with p value of 0.097. One-Way ANOVA showed that the subscales of the PALMS were not statistically significant on the age groups however; identified that physical condition was their motivation towards PA.
Conclusion: This study gave an insight to the PA participation among Malaysians in Gombak district. Health conscious is the primary motive for PA participation among population to prevent non-communicable diseases.

Keywords: Physical inactivity, Motivation, Physical Activity, Non-communicable disease

Optimisation of Off-Loading Footwear (StepEase™) for Diabetic Patients

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Foot wounds are one of the most common and significant complications associated with chronic diabetes. Such wounds can be grouped into several classes including polyneuropathy. The polyneuropathy is a triad of sensory neuropathy, motor neuropathy and autonomic dysfunction. Sensory neuropathy is impaired and/or absent sensation which predispose one to injury. The motor neuropathy may cause weakness or foot deformity which altered the biomechanics of the foot and in combination with sensory neuropathy that cause injury without needing to experience trauma. When walking, a great amount of weight or force is placed on feet. Therefore, an offloading device is required to assist in wound management. StepEase™ is an ergonomic, inspired by nature and friendly user system built to improve the pressure redistribution and gait efficiency properties footwear. It provides a cushioned-structure that when utilised by itself or in conjuction with any socks and/or footwear assemblies will efficiently dissipate and redistribute pressure, thus minimising the chance of ulcer recurrence. It involves configuration of commercial EVA (Ethylene Vynil Acetate) in microball shapes that were packed together allowing a free movement, around its perimeter. The invention is flexible and versatile since it can be developed to suit a wide range of footwears; for outdoors and indoors. Its flexibility to be contour-sensitive is an important consideration in giving extra support to the ulcers and mild foot deformities. In this work, it was found that the thickness of the stuffed EVA had influenced the pressure distribution of the foot, showing the highest reduction of more than 57% on the toes, hallux and metatarsal head areas.

Archery Training Improves Perceived Psychological Status of Sedentary Youth

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Background: Sedentary lifestyle is a major public health issue in Malaysia which not only affecting physical appearance but also psychological characteristics. Impact on the psychological status might influence the perspective of mind especially self-esteem. Therefore, the study objective is to evaluate the effects of 12 weeks intervention of traditional archery training on the perceived psychological status of sedentary youth.
Methods: Thirty-four male youth (18 – 30 years, < 150 min/week moderate to vigorous physical activity) were participated in this study. Subjects were randomly allocated into two groups; intervention and control group. An intervention group (n =17) was involved in a structured 12 weeks archery programme, consisting 3 days weekly. In contrast, a control group (n=17) was requested to perform regular physical activities. The indicator of positive and negative elements in Rosenberg Self-Esteem Score were measured twice; at baseline and after completed the course. Paired T-test was used to examine the study objective.
Results: From the baseline through 12 weeks, self-esteem score for the intervention group showed significant improvement for both positive ($p = .04$) and negative elements ($p= .05$). However, no significant difference was reported for control group in all tested parameters ($p > .05$).
Conclusion: The findings suggest that 12 weeks of traditional archery training programme was effective in improving self-esteem among sedentary youth population. Therefore, traditional archery could be proposed as one of the possibilities method to combat low self-esteem among youth.

Keywords: Traditional archery, self-esteem, sedentary lifestyle, youth

Prevalence of Stress, Anxiety and Depression among Indonesian Women Migrant Workers in Peninsular Malaysia

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Background: Everybody finds it difficult to be away from family. Being apart from family to work in a new environment requires sacrifice, and endeavour to adapt to surrounding which is foreign to them and therefore may cause perturbation and tension. Present study aims to observe the prevalence of mental health problems among Indonesian women migrant workers in Malaysia and its associated factors.
Methods: A cross sectional study was conducted at three representatives of Indonesian Government in Peninsular Malaysia: Indonesian Embassy in Kuala Lumpur, Indonesian Consulate General in Johor Baharu and Penang. Purposive sampling method was used to select respondents who came to the sites to renew their passport. A validated Indonesian DASS 21 questionnaire was performed with Cronbach's alpha 0.9483.
Results: A total of 589 respondents participated and consent granted. The majority of respondents stay in Kuala Lumpur n=107 (18.2%), Selangor n = 117 (19.9%), Penang, n = 168 (28.5%) and Johor Baharu n = 90 (15.3). Participants' age were between 19 to 45 years old (mean age: 27.10 $\pm$ sd. 6.91). Majority of the respondents came from Central Java (n=177, 30.1%), North Sumatra (n=154, 26.1%) and East Java (n=101, 17.1%) respectively. Three-quarters of the respondents' qualification have senior high school level (n=442, 75%), followed by junior high school (n=66, 11.2%), and primary school (n=45, 7.6%). The length of stay in Malaysia was between 1 and 30 years (mean years: 4.19 $\pm$ sd. 3.40). Income range was 500 to 5000 Malaysian Ringgit (mean income:RM1339.95 $\pm$ sd. 452.42). The period of work was between 4 to 21 hours/day (mean period: 11.44 $\pm$ 1.85 hours a day). Most of the workers live in hostels (n=461,78.3%) and were unwed (n=421,71.5%). The measurement of prevalence of stress, anxiety and depression among workers using DASS 21 scale were reported 151 (25.6%), 308 (52.3%) and 139 (23.6%) respectively. Spearman correlation test showed the prevalence of DAS was increased with period work of time in a day and decreased with age and duration of stay in Malaysia. According to

the multivariate logistic regression analysis, younger age was significant predictors of a negative emotional state.
Conclusion: The requirement for further studies such as experimental studies of workers can contribute more solutions to diminish their mental problems.

Keywords: Mental health, DASS, Indonesian women migrant workers, Malaysia

Effects of Stingless Bee Honey (Madu Kelulut) on Bone Metabolism of Glucocorticoid Induced Osteoporosis in Male Rats

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Background: One of the most detrimental effects of prolonged glucocorticoid treatment is glucocorticoid induced osteoporosis. Studies on honey have proven its antioxidant properties that could provide protection against osteoporosis. This study aimed to determine the effect of stingless bee honey supplementation on glucocorticoid induced osteoporosis.
Methods: 46 male *Sprague Dawley* were used, of which 32 rats underwent adrenalectomy and were divided into four groups: non-treated control group (AC, n=8), treated with calcium supplement (PC, n=8), treated with 200mg/kg/day stingless bee honey (KH1, n=8)), and treated with 400mg/kg/day with stingless bee honey (KH2, n=8). The rats were given daily intramuscular Dexamethasone at a dose of 120 g/kg body weight. The remaining 14 rats were divided into baseline (BL, n=6) and sham group (Sham, n=8). Rats in the sham group were injected daily with distilled water. All rats were treated six days a week for two months. Bone densitometry test was carried out six days prior to sacrifice. Upon sacrifice bone tissue was collected for biomechanical strength test.
Results: The PC and KH1 rats had a significantly higher level of serum osteocalcin compared to Sham and AC groups, whereas rats in group KH2 had a significantly lower level of serum Cross Linked C-Telopeptide of Type 1 Collagen (CTX) compared to PC group. Bone densitometry test showed that group KH1 had significantly lower bone mineral density of left femur compared to PC and Sham groups. Some parameters of bone biomechanical strength were preserved in osteoporotic rats receiving stingless bee honey.
Conclusion: Stingless bee honey at a low dose has similar protective effects as calcium in reducing negative effects of glucocorticoids on bone and has potential to be used as an alternative or complementary treatment for glucocorticoid induced osteoporosis.

Keywords: Glucocorticoid, osteoporosis, stingless bee honey

Mislocalisation of Pax7 in Dystrophin-Deficient Myoblasts

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Background: Pax 7 is one of the key factors in the development of tissues and organs during embryogenesis. Previous study has shown that pax7^{+} cell is attenuated in the *mdx* embryo during gestation as well as in dystrophic muscle indicating that an absence of dystrophin in muscle affects pax7 regulation in Duchene Muscular Dystrophy (DMD). Therefore, the objective of this study is to determine pax7 expression patterns in sub- cellular component of dystrophin-deficient myoblasts.
Methods: In this study, dfd13 (dystrophin-deficient) and C2C12 (non-dystrophic) myoblasts were cultured in low mitogen conditions for 10 days to induce differentiation. Differentiation analyses and sub-cellular pax7 expression were achieved via immunofluorescence and immunoblotting. *In silico* analysis were carried out to predict NLS activity of pax7 to further confirm its nuclear localisation.
Results: Our results showed that dfd13 myoblasts did not achieved terminal differentiation as less myotube formation as well as MyHC expression were determined. Pax7 has been found not only localised in the nuclear instead, the pattern of pax7 distribution was mostly perinuclear. Pax7 expression also can be found scattered within the cytoplasm. Sub-cellular localisation analyses showed that pax7 is significantly co- localised higher in endosome as compared to with ER and Golgi which may explaining the extensive dispersion expression within the cytoplasm of dystrophin- deficient myoblasts. In addition, *in silico* inspection of pax7 showed that a predicted bipartite NLS was present in the pax7 sequence, starting at position 134 until residue
220. The scores were 5.8, 5.5 and 5.1, which means that pax7 has intermediate NLS activities, indicating it could be localised within both the nucleus and cytoplasm.
Conclusion: Collectively, it was established that more pax7 is localised in the cytoplasm indicating the mislocalisation of pax7 where it may undergo protein modification and be recycled in proliferating dystrophin-deficient myoblasts attributed to myogenesis impairment.

Keywords: Pax7, dystrophin-deficient myoblasts, myoblasts differentiation, muscular dystrophy

Potential Applications of Chitosan-based Nanoparticles in Treating Diabetic Wounds

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Background: Chitosan-based nanoparticles (CSNPs) have attracted great interests as versatile drug delivery vehicles due to their good properties and biological effects, including biocompatible, non-toxic and having anti-bacterial as well as anti-oxidant effects. CSNPs have also been extensively investigated as drug carriers for topical delivery, particularly for treating diabetic wounds. Thus, the ability of CSNPs to deliver active agents with different modes of action were studied for the management of diabetic wounds. Curcumin (Cur) and Dicer-substrate small interfering RNA (DsiRNA) were used in this study due to anti-inflammatory and antioxidant activities of Cur and the ability of DsiRNA to inhibit expression of prostaglandin transporter (PGT) gene which resulted in vascularization and promotion of wound healing.
Methods: CSNPs were loaded with Cur and PGT DsiRNA via ionic gelation method to produce multi-action formulation. Chitosan was also used as stabilizing agent in the biosynthesis of gold nanoparticles (AuNPs) using extracts of "Tiger milk mushroom" (*Lignosus rhinoceros*) which later adsorbed with DsiRNA to provide antibacterial and wound healing effects. Both formulations were characterized for their physicochemical characteristics and incorporated into topical formulations prior to determination of their biological effects in *in vitro* and *in vivo* studies.
Results: The particle size of Cur-DsiRNA loaded CSNPs and chitosan stabilized AuNPs were less than 500 and 100 nm, respectively. Both were positively charged (>30 mV) and able to load high percent of active agents. An in vivo study showed that the optimized topical formulation of Cur-DsiRNA loaded CSNPs resulted in faster healing of diabetic wound compared to controls. On the other hand, chitosan-stabilized AuNPs displayed effective antibacterial activity against gram-negative (*Pseudomonas aeruginosa* and *Escherichia coli*) and gram-positive bacteria (*Staphylococcus aureus* and *Bacillus sp.*) as determined by disc diffusion assay.
Conclusion: Both nanoparticles had shown great potential to be further developed as topical formulations in treating diabetic wounds.

Keywords: Nanocomposites, antibacterial agent, diabetes, drug delivery, RNA interference

Annatto Derived Tocotrienol Enhanced BMP-2 Protein by Inhibiting Rhoa Activation and HMG-CoA Reductase Gene on MC3T3-E1 Cells

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Background: Annatto-derived tocotrienol contains 100% tocotrienols (90% δ-tocotrienol and 10% γ-tocotrienol) and has been shown to have osteogenic activity in preosteoblastic cells. In this study, we aimed to elucidate the effects of AnTT on bone morphogenetic protein-2 (BMP-2), RhoA activation and HMG-CoA reductase gene in murine preosteoblastic cells.
Methods: MC3T3-E1 cells were cultured with cell density of $1x10^4$ cells/mL and incubated overnight in growth media (α-MEM + 10% serum). On the next day, the media was changed with various concentrations of AnTT (0.001 – 1 µg/mL) in differentiation media (DM; growth media + 3 mM sodium phosphate + 50 µg/mL ascorbic acid). Ethanol was diluted in DM and used as vehicle. AnTT treatments were changed every 2-3 days. For RhoA activation and BMP2 protein, the cells were treated for 9 and 15 days. Cell lysates were collected and ELISA assays were performed. For gene expression, the cells were incubated for 3, 9, 15 and 21 days. RNAs were extracted and gene expression was measured using RealTime PCR method. Lovastatin was used as positive control.
Results: Lovastatin significantly increase BMP-2 protein (day 15) and inhibit RhoA activation (day 9 and day 15) ($P<0.05$). HMG-CoA reductase gene was down-regulated at day 21 in lovastatin group. On the other hand, AnTT at 1 µg/mL significantly increase BMP-2 protein at day 15 compared to vehicle ($P<0.05$). The 0.1 µg/mL AnTT group significantly decrease RhoA activation at day 9 compared to vehicle ($P<0.05$). The 0.001 µg/mL (day 9) and 0.1 µg/mL (day 21) AnTT significantly down-regulate HMG-CoA reductase gene expression compared to vehicle ($P<0.05$). At day 21, HMG-CoA gene expression was significantly reduced in all groups compared to day 15.
Conclusion: Annatto tocotrienol inhibits RhoA activation which leads to increase of BMP-2 protein in preosteoblastic cells. In addition, AnTT also down-regulate HMG-CoA reductase gene. These changes predispose to osteoblast differentiation and anabolic bone growth.

Keywords: Tocotrienol, bone, vitamin E, osteogenic, osteoporosis

Metal-Ceramic Composite for Medical Application: Screw

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Background: Ti6Al4V is widely used in many applications due to satisfactory mechanical properties, excellent corrosion resistance and low density. However the bioinertness and poor osseointegration properties of Ti6Al4V limits its application for implantation purposes. On the other hand, Hydroxyapatite (HA) usually used as coating in biomedical industry to promote osseointegration between bones and orthopaedic implants. Therefore it would be interesting to design a metal based-ceramic composite by using Ti6Al4V and HA as second phase constituents. The presence of HA between Ti6Al4V matrices to enhance the bioactivity of Ti6Al4V without comprising the mechanical set properties of Ti6Al4V. The objective of this study is to fabricate fixator screw made up from Ti6Al4V/HA composites by PIM. PIM is well known for its capability to obtain desired complex shape with nearly full density and its applications include complex shape machine parts, medical devices parts, automotive parts and high temperature applications.
Methods: Ti6Al4V and HA were characterized by scanning electron microscope (SEM), X-Ray Diffraction Analysis (XRD) as well as particle size analysis. 90 wt% Ti6Al4V and 10 wt% HA were mixed 60 wt% palm stearin and 40 wt% polyethelene to obtained their feedstocks. Subsequently, the obtained feedstock was passed through the capillary rheometer to determine flow behaviour of the feedstock.
Results: Based on rheology study, Ti6Al4V/HA feedstocks was identified as pseudo-plastic or shear thinning and the activation energy is 10kJ/mol.
Conclusion: Flow behavior and viscosity of the feedstock relies on characteristics of the powder as well as its packing density. The addition of small particles of HA in the Ti6Al4V not only to enhance bioactivity of the Ti6Al4V but also to increase the packing density of feedstock. This will lead to better shrinkage during sintering as well as composites density. High density obtained will resulted in good mechanical properties such as hardness value, bending strength and Young Modulus.

Keywords: Ti6Al4V/HA, PIM

Factors Associated with Self-Esteem among Adult Male Inmates in a local Prison Malaysia

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Background: Self-esteem refer to confidence and satisfaction in oneself and an important determinant of psychological well-being among inmates. Nevertheless, hardly any studies examined self-esteem among local prisoners. Therefore, the objective of this study was to determine the prevalence and association between low self-esteem and socio-demographic characteristics, biological influences, psychological factors, childhood related experiences and offence related history among adult male inmates.
Methods: A cross sectional study was conducted in a local prison in peninsular Malaysia. Questionnaire was distributed to 507 inmates using proportionate random sampling to answer the structured questionnaire. Self-esteem which was the dependent variable, measured using pretested and validated Rosenberg self-esteem scale which categorized into high and low self-esteem. Chi-square and logistic regression analysis were applied to determine the association between the variables. Analysis was done using SPSS version 22.0. Adjusted odds ratio with its 95% confidence interval was used to identify correlates of self-esteem while level of significance was set at $p<0.05$.
Results: Out of 507 respondents, 460 completed the questionnaire (response rate 90.7%).The overall mean self-esteem score was 37.80 $\pm$ 5.70 from a possible 10 to 50 total score. The prevalence of low self-esteem was 38.3%.There was a significant relationship between self-esteem and presence of children, presence of visitors, highest level of education and marital status ($p<0.05$). Factors associated with self-esteem was ever married (OR= 1.70; 95% CI 1.17 to 2.50; $p=0.006$) and presence of children (OR= 1.48; 95% CI 1.02 to 2.17; $p=0.041$).
Conclusion: Results showed no significant association between self-esteem and modifiable factors. Larger scale studies need to be carried out with various modifiable variables so that we can identify predictors that can be used as an intervention to increase self- esteem among inmates. This is important to create awareness among prisoners about his life's self-worth and improve psychological wellbeing.

Keywords: Self-esteem, Adult, Inmates, Prison, Malaysia

Qualitative Analysis: Issues Concerning Medication Management in Residential Aged Care Facilities (RACF)

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Background: Malaysia is one of many developing countries in the world that faces the issue of an increasing older population. Co-morbidity of non-communicable diseases and multiple medication usage among older persons is the norm for this population. Medication management at residential aged care facilities (RACFs) or nursing homes has become increasingly more important in providing quality care for the health of residents.
Methods: A qualitative study was conducted to identify the relevant barriers in achieving effective medication management in these settings. The duration of data collection in this study was from March until October 2017. Analyses in the form of documents from published journals, analytical writing, journal keeping, policy report or press releases were utilised. By incorporating keywords and searching various documents of multiple databases including Mendeley, Medline, Science Direct, Google and Google Scholar, the extracted data was analysed using thematic analysis to classify and find the pattern of issues. The triangulation method emphasised within method and type of investigator was used to validate the data.
Results: Several themes surfaced including governance associated with medication management, regulatory, system influenced medication management, medication use process, theory of interdisciplinary collaboration, patient-related factor, staff-related factor and lack of research on medication management were identified in this study. The validated data is important to discover the barriers in achieving good medication management.
Conclusion: Thus, the finding in this study highlighted the issue regarding medication management requiring standardised system and established guideline

Keywords: Qualitative analysis, nursing home, residential aged care facility, long-term care, medication management

Automatic Detection and Counter for Lymphoblast Cell

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Background: Acute lymphoblastic leukemia (ALL) is a common cancer which is normally suffered by children. ALL is caused by the increasing number of lymphoblast cell in the blood which is produced by the bone marrow. Lymphoblast cell is an immature lymphocyte cell (a type of white blood cell). In order to identify whether the patient is suffered from ALL disease, Laboratory Haematologist have to examine and calculate the percentage of lymphoblast cell in the blood film on the glass slide under microscope manually which is time consuming. Thus, a research was carried out to build a system that helps haematologist in analysing and identifying the lymphoblast cell, reducing time taken without compromising the effectiveness of work.
Methods: This system uses image processing technique to enable a computer to analyse and identify the lymphoblast cell in peripheral blood film. Images of ALL blood samples obtained from Hospital Chancellor Tuanku Muhriz were captured with digital microscope at 20X magnification. In this research, images were converted into grayscaled and box filtering with 3*3 pixel window size and rescaling were used for noise filtering and masking. Then, Hough Circular Transform technique were used to extract circular and size feature in classifying lymphoblast cell. With total of 100 images, 70 images were used or training and the balanced were used for testing the classification model.
Results: The accuracy of lymphoblast cell counted were used to measure the system's performance. Out of 30 test images, we managed to get 86% accuracy with 92.5% true positives and 0.925 sensitivity score.
Conclusion: This research has proved that with correct image processing techniques and good machine learning approach, lymphoblast cells can be detected and counted, reducing some of the Haematologist workload. The performance however, could be further improve with colour and texture features of the detected lymphoblast. In addition, Support Vector Machine or Deep Learning might also improve the classification result.

Keywords: Lymphoblast Detection, while blood cells, digital pathology

Automatic Leucocytes Detector, Classifier and Counter.

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Background: White blood cells, or leucocytes, are a type of immune system cells in the human body. The amount and type of white blood cells in a human body can determine the health of a person. A Laboratory Haematologist, who prepares a blood film on a slide from peripheral blood sample will observe it under a microscope to determine the type and percentage of leucocytes in the patient's blood. Therefore, a system to detect, classify and count Leucocytes into granulocytes and agranulocytes would be developed to assist Haematologist in this tedious but routine task. This research will focus on determining the characteristics of leucocytes from its images, for classification and counting purposes.
Methods: 100 blood film images with 20X magnification were captured using a digital microscope. Images are then converted into grayscale images using threshold value of 170 for perfect binary images. Images were then filtered with median filtering techniques using 5x5 pixels mask for noise removal, leaving only leucocytes in images. A shape finder algorithm was implemented to find blobs in the image as candidate leucocytes. Rectangular area around the candidate leucocytes will be treated as regions of interest. Finally, a fine-tuned Hough Circle transform algorithm was applied to detect finer circular objects within these regions of interest and a classifier was used to classify objects with certain features as agranulocytes while those without as granulocytes.
Results: The software yields an accuracy of 96.03% in detecting and counting leucocytes and an accuracy of 76.78% in classifying leucocytes into granulocytes and agranulocytes.
Conclusion: The research not only managed to use basic image features to identify leucocytes from a normal red blood film, but further classify them into granulocytes and agranulocytes. However, a further research need to be carried out to polished the granulocytes and agranulocytes result, including venturing into colour features.

Keywords: Leucocyte Detection, Leucocyte Classification, Digital Pathology

Quantification of Paracrine Factors of Nasal Fibroblast that Enhance Airway Epithelial Cells Wound Healing

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Background: The nasal fibroblast (NFs) secretome, which comprises various cytokines, chemokines, angiogenic factors, and growth factors, synergistically promote the respiratory epithelium restoration and regeneration after injury. However, critical role of proteins and other products secreted by NF on respiratory epithelium wound healing have not been studied extensively. This study was undertaken to profile and quantitate the proteins secreted by NFs that can enhance the wound healing of airway epithelial cells (AECs) to identify the key factors in the secretome.

Methods: Human nasal epithelial cells and NFs were isolated from consented patients undergoing turbinectomy and co-cultured. NFs were differentially trypsinized, leaving the colonies of AECs to reach confluency. For conditioned medium collection, the fibroblasts at passage 2 was cultured with F-12: Dulbecco's Modified Eagle's Medium (FD) + 10% fetal bovine serum (FBS) until it reach 90% confluency before the culture medium is changed to either serum free airway epithelial cell basal medium (AE) or serum free FD and maintained for three days for the collection of NF conditioned medium, denoted as AECM and FDCM, respectively. AECM and FDCM, each from 5 human samples has been collected and pooled for all the analysis. The secretomes were concentrated, precipitated, quantified and analyzed on SDS-PAGE before sample preparation for protein identification followed by protein quantification by mass spectrometry analysis.

Results: Optimization of seeding density showed that 7,500/cm is the best cells seeding density to analyze the effect of the AECM and FDCM on the AECs proliferation. Migration assay showed that AECM enhanced the RECS migration compared to complete airway epithelial cell medium, alone. The conditioned media that has been collected is currently have been sent for quantitative mass spectrometry analysis.

Conclusion: Protein identification followed by protein quantification by mass spectrometry analysis will enable identification of key secreted factors of NFS that enhance wound healing of AEC.

Keywords: Respiratory epithelium, conditioned medium, migration, secretome

The Potency of Several Dietary Chemicals in Inducing Heme Oxygenase-1 Expression in Mice Liver

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Background: Heme oxygenase-1 (HO-1) is an enzyme that possesses anti-oxidant, anti- inflammatory and cytoprotective functions. Induction of HO-1 occurs as an adaptive and beneficial response to various injurious stimuli such as oxidative stress. The objective of this study was to determine the potency of sulforaphane, curcumin, quercetin, indole-3-carbinol and butylated hydroxyanisole in inducing the expression of HO-1 gene in mice liver.
Methods: 48 adult male ICR white mice (25–30 g) were divided into 8 groups: normal control group (n=6), sulforaphane treated group (n=6), quercetin treated group (n=6), curcumin treated group (n=6), butylated hydroxyanisole treated group (n=6), indole-3-carbinol treated group (n=6), vehicle 1 control group (n=6) and vehicle 2 control group (n=6). All chemicals were administered intraperitoneally at a dose of 50 mg/kg for 14 days. Vehicle 1 (DMSO, Tween 20 and normal saline at a ratio of 0.05:0.1:0.85) was used to dissolve sulforaphane, quercetin and curcumin. Vehicle 2 (corn oil) was used to dissolve indole-3-carbinol and butylated hydroxyanisole. At day 15, the animals were sacrificed and their livers were isolated. From the liver, total RNA was extracted, reverse transcribed and subjected to quantitative real-time PCR to detect HO-1 gene expression. Agarose gel electrophoresis was also performed to verify the specificity of the amplification.
Results: The results showed that HO-1 gene expression levels were significantly increased by 4.6, 3.6, 3.6, 3.3 and 3-fold after treatment with 50 mg/kg of sulforaphane, indole-3- carbinol, butylated hydroxyanisole, curcumin and quercetin respectively, as compared to controls ($p<0.05$).
Conclusion: At a dose of 50mg/kg administered for 14 days, sulforaphane was the most potent in inducing HO-1 gene expression in mice liver, while quercetin was the lowest.

Keywords: Heme oxygenase-1, dietary chemicals, gene expression

Chlorella vulgaris Improves Muscle Strength and Function by Combating Oxidative Stress in Young and Old Sprague Dawley Rat

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Background: *Chlorella vulgaris* is a green eukaryotic microalga that has been reported with numerous pharmacological benefits. In this study we aimed to determine the effects of *C. vulgaris* in combating oxidative stress in young and old Sprague Dawley (SD) rats.

Methods: Thirty SD rats aged 3 months (young) and 21 months (old) were divided into three groups; Group 1 (untreated control) was given distilled water, Group 2 was treated with 150 mg/kg body weight (BW) of *C. vulgaris*, and Group 3 was treated with 300 mg/kg BW of *C. vulgaris*. Treatment with *C. vulgaris* was carried out by oral gavage for three months. Grip strength of front and hind paws and muscle function were determined on Day 0, 30, 60 and 90 of treatment. Urine and blood of each rat were collected on Day 0 and Day 90 of treatment. On Day 91, all rats were sacrificed and gastrocnemius muscles were collected. Urine and plasma samples were measured for 15-isoprostanes F_{2t} activity by Urinary Isoprostanes ELISA Kit (Oxford Biomedical Research, Oxford, USA) and creatine kinase-MM (CKMM) activity by Rat CK-MM ELISA Kit (Life Diagnostics Inc, West Chester, USA). Measurement of skeletal muscle oxidative stress was performed by using Bioxytech® LPO-586™ Assay Kit (Oxis Research, Oregon, USA).

Results: The grip strength of front and hind paws of *C. vulgaris*-treated rats was significantly increased on Day 30, Day 60 and Day 90 compared to Day 0. A similar increase in grip strength of front and hind paws was observed in *C. vulgaris*-treated rats on Day 30, Day 60 and Day 90 compared to untreated control on the same respective days ($p<0.05$). For muscle function, total path was significantly increased for rats treated with 300 mg/kg BW of *C. vulgaris* on Day 60 and Day 90 compared to Day 0. No significant difference was observed between young and old rat on Day 0 for isoprostanes F_{2t} urinary oxidative stress. However, young and old *C. vulgaris*-treated rats demonstrated a significant decrease in isoprostanes compared to its respective control on Day 90. The plasma CKMM was significantly increased in old rats compared to young rats on Day 0 and

was significantly decreased in young and old *C. vulgaris* treated rats compared to its respective control on Day 90. A significant increase in malondialdehyde (MDA) and 4-hydroxyalkenals (HAE) levels were observed in control old rats compared to control young rats. However, a significant decrease in the levels of MDA and HAE were observed in both young and old rats with *C. vulgaris* treatment.
Conclusion: *Chlorella vulgaris* enhances muscle strength and function by combating oxidative stress in young and old Sprague Dawley rat.

Keywords: *Chlorella vulgaris*, muscle strength, muscle function, oxidative stress

Case Study: Bed Management Mobile Application for Hospital Canselor Tuanku Muhriz

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Background: Bed management is one of the crucial operation in a hospital. The current desktop-based system in Hospital Canselor Tuanku Muhriz (PPUKM) is designed for user to perform different routine tasks to assists the hospital operation. The fix location and amount of desktop computer (PC) in PPUKM have created some difficulties to efficiently manage the beds (i.e. one of the crucial factor that cause delay in allocating beds to patients). Mobile offers few benefits especially the mobilize characteristic where user can access the system at anywhere and anytime. Hence, this research is to study the applicability of a mobile-based application for the bed management.
Methods: Qualitative data collection method such as observation and interview with expert user (nurse, doctor and system developer) and analysis on the existing system have been done to acquire the user requirement for designing the mobile-based application for bed management. Some important features are login, bed information visualization based on the discipline and ward, bed information updating and ward information updating modules. A user experiment study with 150 participants was conducted to evaluate the applicability of the mobile application.
Results: 81.74% respondent using Android while 18.26% respondent using iOS. The mean value for usefulness, ease of use and satisfaction factors from the questionnaire with 1-5 Likert scale are 3.37 (Good) ,3.35 (Good) and 3.36 (Good). 84.21% from the 57 respondents given positive feedback that they agree the app will facilitate their job in term of ease their job, information sharing is fast and easy as well as time saving. Meanwhile, respondent also concern about the Internet and data consumption of the app which take up 45.83% in the negative feedback.
Conclusion: The study suggested a positive feedback about that the mobile application to be embedded with the existing system in the bed management operation.

Keywords: Bed management, Mobile Application

Preparation of Fibrinogen-depleted Human Platelet Lysate for Cell Culture Purposes

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Background: Culture medium for stem cells is usually supplemented with human platelet lysate (HPL), human serum or foetal bovine serum. These supplements are essential as they modulate the survival, proliferation and migration of cells in culture. HPL is ideal for the expansion of cells for clinical application. However, problems arise when using HPL prepared from platelet concentrates via repeated freeze-thaw cycle and centrifugation as the chances of clot formation in culture is high. In this study, we test a simple and inexpensive method to remove fibrinogen from the HPL to minimize the possibility clot formation.
Methods: We prepared the HPL by pooling 2-4 bags of expired platelet concentrates and then lyse the plasma membrane via repeated freeze-thaw cycle. Then, fibrinogen was depleted by adding different concentrations of calcium chloride and heparin, followed by incubation in 37˚C for 2 hours and 4˚C overnight. Fibrin clots formed were removed via centrifugation to prepare the fibrinogen-depleted human platelet lysate (fdHPL). To determine the quality of the fdHPL, fdHPL were kept in 4˚C for 7 days to examine clot formation. Clot formation in fdHPL supplemented culture medium was also analysed.
Results: Addition of calcium chloride, with or without heparin, resulted in the formation of fibrin clot than can be removed after centrifugation. Clot can be seen with eye by day 3 except for the groups added with calcium chloride alone. Microscopically, fdHPL without heparin also showed lesser debris and clot formation. Importantly, no clot was seen in medium supplemented with these fdHPL.
Conclusion: We successfully prepared fdHPL that does not clot in medium. However, more studies need to be conducted to determine the quality and functionality of the fdHPL.

Keywords: Fibrinogen, platelet concentrate, human platelet lysate, cell culture, cell therapy

Effect of *Zingiber officinale* Supplementation on Muscle Strength and Performance of Young Male Sprague Dawley Rats

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Background: *Ginger (Zingiber officinale) which is* rich in gingerol and shagaol has been known for its hypoalgesia effects besides having antioxidant and anti-inflammatory properties. This study aimed to determine the effects of ginger on muscle strength and performance in young rats.
Methods: Three-month old male Sprague Dawley rats were treated with either distilled water (n=10) or ginger water extract (n=8) at concentration of 250 mg/kg body weight daily for 3 months via oral gavage. Muscle strength and function as well as bone mineral density were assessed at day 0, 30 and 60 of treatment. Muscle strength assessment included whole body, front and hind paws grip strength which were measured by using Bioseb Grip Strength Test (Pinellas Park, USA) while muscle function was assessed by open field test. Bone mineral content (BMC), bone mineral density (BMD), fat percentage (% fat) and fat free mass (FFM) were measured to represent muscle integrity by scanning using 'dual energy X-ray absorptiometry' (DEXA) machine (Hologic, Bedford, USA).
Results: Ginger supplemented rats showed a significant improvement in forelimb muscle strength as early as day 30 of supplementation. However, open field test which assessed the locomotor activity, showed no significant difference in total distance travel and speed of moving with ginger supplementation. BMC, BMD, % fat and FFM were not changed in ginger supplemented rats.
Conclusion: Our study highlighted the potential of ginger supplementation in improving muscle strength in young rats thus, can be used as an intervention strategy for delaying sarcopenia progression.

Keywords: *Zingiber officinale*, ginger, muscle strength, muscle performance, young rats

Stroke Recovery Assesment Based on Kinematic Profiling Using Simplified Video Processing Method

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Background: The purpose of the study was to analyse and develop a profile of kinematics parameter for a hemi paretic stroke subjects based on reaching activity using simplified video analysis method

Methods: Six subjects were divided equally into three different groups which are recovery, half recovery and non-recovery, as to observe the different characteristic performed by each group. Subjects were asked to perform three trials reaching activity starting from rest position to reach a cylinder object size in front of them and pull back to the initial rest position, two video cameras were used to capture the left and right side of the subject and to record the reaching movement. From the video analysis, the kinematics variables of displacement, velocity, acceleration, angular displacement, angular velocity and angular acceleration were measured.

Results: The comparison analysis were done between this groups based on the kinematic values on each group using statistical analysis which are maximum value, mean value and the standard deviation value. The finding from the comparison analysis showed there are five parameter of reaching movement that differentiate the unique character of recovery, half recovery and non-recovery movement. The parameters are (1) efficient movement (shorter movement time), (2) straight movement travelling pattern (less total displacement and travelling distance), (3) smooth movement (velocity and acceleration, (4) stability (lower standard deviation for displacement and velocity) and (5) optimisation movement (high angular value). From the five parameter, Two selective significant parameter was choose from the principal component analysis (PCA) that can rank the significant parameters value that will be used as a profile characteristic for a recovery, half recovery and non-recovery stroke patient.

Conclusion: The profile for each group then can be used as a reference model to check the real time result of recovery level for the stroke patient. The modelling also can be applied to any activity conducted by the stroke patient to class the current condition of the stroke patient.

Keywords: Kinematic, stroke recovery, simplified video processing, stroke profile

Anatomical and Physiological Investigation of Pathways Mediating the Effects of Electrical Stimulation of the External Auricle of the Ear on Autonomic Nervous System Activity in Rats

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Background: Heart failure is a debilitating condition that commonly associated with autonomic nervous system dysfunction. It has been recognized hyper activation of the sympathetic nervous system together with impaired vagal tone further worsened the cardiovascular disease. As such, activation of the auricular branch of the vagus nerve (ABVN) through electrical stimulation has been shown to provide cardio protection against a failing heart. It is our interest to investigate the pathways mediating the effects of electrical stimulation of the external auricle of rats, comparing an ABVN innervated site of the external ear (the tragus) to an area not reported to receive ABVN innervation, the earlobe.
Methods: In anatomical investigation, young male Wistar rats (65-85g) were deeply anaesthetised with a 4% mixture of isoflurane in oxygen. For each animal, a total of 5 µl of 20 mg/ml CTB in 0.1 M phosphate buffer saline (PBS) was injected on right tragus (n=4) and right ear lobe (n=4) at using a glass microelectrode. The animals were allowed to recover for 3-4 days prior to being humanely and proceed for immunohistochemistry. Electrical stimulation (100 Hz, 2.5 mA) was delivered for 5 minutes into the auricular stimulation sites in pre-weaned Wistar rats (18 – 21 days). The physiological responses upon select auricular stimulation were performed in the Working Heart Brainstem Preparation (WHBP). In brief, the animals were decerebrated at pre-collicular level, skinned, thoracotomized. Animals were cannulated and perfused with carbogenated artificial cerebrospinal fluid. The phrenic nerve and lumbar sympathetic chain were attached to suction electrode and the nerve activities were directly recorded.
Results: Afferent terminals were predominantly labelled ipsilateral to the injection site, with the densest labelling within laminae III-IV of the dorsal horn of the upper cervical spinal cord. In the medulla oblongata, CTB labelled afferents were observed in the paratrigeminal nucleus, cuneate nucleus, and to a minor extent in the nucleus tractus solitarius. Direct recording from the sympathetic chain revealed a central sympathoinhibition from both tragus and earlobe stimulation. Sectioning of upper cervical afferent nerve roots silenced the sympathoinhibitory effects of

tragus stimulation.
Conclusion: Considering the predominance of afferent labelling in the cervical spinal cord dorsal horn and that cervical afferent nerve section reduced the sympathoinhibition evoked by tragus stimulation, this suggests that the autonomic effects of auricular stimulation are conveyed through somatosensory afferents rather than the ABVN.

Keywords: Transcutaneous vagus nerve stimulation, autonomic nervous system, working heart brainstem preparation, heart failure

Dual-Crosslinked Gelatin Bioactive Scaffold as a Potential Acellular Treatment for Diabetic Foot Ulcer

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Background: The chronic wound recently increases the morbidity rate among Asian population especially Malaysia which involved the diabetic foot ulcer. In the worst-case scenario, a diabetic patient could be amputated and end-stage-renal-disease (ESRD) that causing death. The wound care management of the ulcer is critical to support the wound healing and avoid the bacterial infections. Thus, this study aimed to develop a potential acellular treatment consist of the natural-based biomaterial crosslinked with a natural crosslinker.
Methods: Briefly, the gelatin powder was dissolved in distilled water at -40˚C for 30 minutes. The gelatin solution was pre-frozen at -80˚C for 6 hours followed by the freeze- drying process. Gelatin scaffold (GS) was post-crosslinked with genipin (GNP) and followed by carbodiimide (EDC) for 6 and 12 hours, respectively. The physico-chemical, mechanical strength properties followed by cellular compatibility were tested. Besides, the toxic effect of fabricated GS was tested with human dermal fibroblasts (HDF) via live & dead assay.
Results: The results demonstrated the heterogenous porous structure (more than 80%) and its pore size range between 100-200 µm. The fabricated scaffold with dual crosslink effect showed higher crosslinking degree and promoted slow degradation. It also described no different for swelling ratio and gas transfusion properties compared to non-crosslink. There had no change in the elements composition (EDS), chemical structure (FTIR) and atomic arrangement (XRD) for the non- and post-crosslink of GS. However, the thermogravimetric (TGA) and mechanical strength (6-7 Mpa) showed higher on crosslinked-GS than that of the non-crosslink. Both crosslinked-GS and non-crosslink unravelled no toxic effect on the post-seeding of HDF.
Conclusion: In conclusion, the dual-crosslinked GS has a potential healing effect on the current chronic wound management of foot diabetic ulcer in term of enhancing tissue regeneration.

Keywords: Gelatin, Acellular, Genipin, Bioactive scaffold, Diabetic ulcer

An Updated Review: Proton Pump Inhibitors and Bone Fracture Risk

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Background: Proton pump inhibitors (PPIs) are commonly prescribed to patients having gastric acid-related disorders. Multiple studies report that the use of PPIs is associated with an elevated fracture risk, especially at the wrist, hip and spine. However, the causal relationship between PPIs and fracture risk remains controversial. Therefore, this systematic review aimed to examine existing longitudinal data on the relationship between PPIs and fracture risk.
Methods: A literature search was performed from 1/8/2018 to 31/8/2018 with PubMed, Scopus and Web of Science using keywords ("proton pump inhibitors" OR omeprazole OR pantoprazole OR "acid suppress*") AND (fracture OR osteoporosis OR osteopenia OR bone). All original research articles published from the year 2013 onwards were considered. Only original research articles written in English with the main objective to study the relationship between PPIs and the risk of fractures were included in this review. This review only included longitudinal or prospective cohort studies. Two reviewers decided the articles to be included in the review.
Results: A total of 18 articles, which fulfilled the criteria and provided sufficient information for data extraction, were included for this review. Majority of the studies are conducted in the Western countries. The studied populations included Alzheimer's patients, stroke patients, elderly, men and postmenopausal women. The mean follow-up period ranged from 3.45 to 14.4 years. Most studies assessed hip fracture while a few studies reported multiple fracture sites. Overall, PPIs were associated with an increase in fracture risk in multiple studies (n=13) although some studies show no significant relationship (n=5).
Conclusion: There is strong evidence suggesting a significant relationship between the use of PPIs and the risk of fractures. Therefore, prophylaxis should be considered in patients on long-term PPIs to decrease the risk of fractures.

Keywords: Bone, Compression, Omeprazole, Osteoporosis, Pantoprazole

Palm Tocotrienol in the Prevention of Cellular Ageing of Human Myoblasts

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Background: Ageing results in loss of muscle mass and strength. Myoblasts play an important role in maintaining muscle mass through regenerative processes, which are impaired during ageing. This study aimed to determine the effects of the tocotrienol-rich fraction (TRF) in promoting myogenic differentiation hence protecting myoblasts from cellular ageing or replicative senescence.
Methods: Primary human myoblasts were cultured into young and senescent stages and were then treated with TRF for 24 h, followed by analysis of cell proliferation, senescence biomarkers, cellular morphology and differentiation.
Results: Cellular ageing or replicative senescence impaired the regenerative capacity of myoblasts, resulting in changes in cellular morphology, cell proliferation, senescence-associated β-galactosidase (SA-β-gal) expression, myogenic differentiation and myogenic regulatory factors (MRFs) expression. Treatment with TRF increased BrdU incorporation in senescent myoblasts, and promoted myogenic differentiation through the modulation of MRFs at the mRNA and protein levels. *MYOD1* and *MYOG* gene expression and myogenin protein expression were modulated in the early phases of myogenic differentiation. TRF treatment also improved the morphology of senescent myoblasts, increased cell viability and decreased SA-β-gal expression.
Conclusion: Tocotrienol-rich fraction promotes myoblasts differentiation by modulating MRFs expression indicating vitamin E potential in the modulation of replicative senescence of human myoblasts

Keywords: Palm tocotrienol, cellular ageing, myoblasts differentiation, myogenic regulatory factors, myogenin

A Comparison of Different Proteases in Generating the Proteomics Map of the Livers of Hypertensive SHR Rats

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Background: The use of only a protease, i.e. trypsin impedes the coverage of protein sequences in proteogenomics. This is because some of the peptides generated by trypsin may be physically or chemically not amenable to LC-MS/MS analysis. Therefore, we applied five commercial proteases, i.e. trypsin, Lys-C. Glu-C, Asp-N and chymotrypsin to digest the liver tissue of a rat of the SHR (spontaneous hypertensive rat) strain.
Methods: Rat liver tissues were pulverized in liquid nitrogen in 8 M urea/thiourea and divided into 5 equal portions to be digested with five abovementioned proteases. Each aliquot was fractionated using strong cationic exhange (SCX) chromatography into 26 fractions that were subject to LC-MS/MS. Raw files from LC-MS/MS were analyzed with Proteome Discoverer version 1.4 against a in-house ENSEMBL database assembled from next-generation sequencing (NGS) of the genome and transcriptome of the SHR rats. Finally, the number and coverage of the peptides generated, as well as the variants such as SNPs, indels and spliced sites covered by each enzyme were evaluated.
Results: We obtained peptide evidence for 21,803 proteins. Besides, our data provide support for 337 unique peptides matching 120 novel splicing events; and 190 unique peptides match with allele-specic sequences. Importantly, 54 out of a possible 196 non- synonymous RNA-editing events could be confirmed by unique peptide-based evidence.
Conclusion: By combining five proteases instead of only trypsin, we demonstrate that both sequence coverage and number of peptides identified can be enhanced considerably. This allows us to pin-point the variant sites (SNPs, mutations, RNA-edits and spliced junctions) better using proteomics technology.

Keywords: Proteogenomics, Trypsin, spontaneous hypertensive rat (SHR)

Markers of Vascular Function among Obese Malaysian Men

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Background: Obesity is associated with increased risk of cardiovascular disease (CVD). Pulse wave velocity (PWV) and augmentation index (AI) are markers of vascular function and are associated with CVD. The studies on the relationship between obesity and these markers are still lacking. The study aimed to determine the association between obesity and vascular function among urban Malaysian men.

Methods: 307 men aged more than 39 years old were recruited from Klang Valley, Malaysia. Their weight, height, waist circumference (WC), blood pressure (BP), PWV, AI, blood sugar (FBS) and blood cholesterol were measured. Obesity was defined as body mass index (BMI) $\geq$27.5 kg/m^2. The subjects were divided into obese group (OG, n=90) and non-obese group (NG, n=217). Data were analyzed by using SPSS version 16.

Results: OG had higher BMI (30.74 $\pm$ 2.89 vs. 23.27 $\pm$ 2.41 kg/m^2), WC, central and peripheral BP, FBS, triglyceride and lower high density lipoprotein when compared to NG. After adjustment for other CVD risk factors, OG had higher AI (16.89 $\pm$ 5.96 vs. 16.18 $\pm$ 5.74%, P<0.05) when compared to NG. No different was observed for PWV (8.70 $\pm$ 1.27 vs. 8.47 $\pm$ 1.42 m/s, P>0.05) between the groups.

Conclusion: Obesity is associated with increased AI. Increased in AI may be one of risk factors predisposing obese subjects to CVD.

Keywords: Obesity, pulse wave velocity, augmentation index, Malaysian men

Antibiofilm Strategies for Combating Infections in Diabetic Chronic Wounds

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Graphene is a carbon crystal with a 2-D lattice structure and has extraordinary properties including exceptional mechanical strength and stiffness, and extreme chemical stability. Recently, graphene oxide (GO) have attracted attention in scaffold substrates for tissue regeneration and carriers for drug or gene delivery. It was shown that GO exhibits proangiogenic activity, observed by several in vitro and in vivo assays. This made GO a potential material for the development of wound dressing. Collagen is usually considered as an ideal biomaterial for wound dressings applications. However, the poor mechanical property of collagen hydrogel limits their applications to some extent. Regarding epidermal growth factors (EGF), there are several commercially available EGF for wound healing but the major disadvantage about these is that it requires continuous administration (at least every 12-24h) or high doses to exert the desired effects due to the low GF in vivo stability. To overcome this, it is crucial to develop a GO based collagen wound delivery system which is mechanically strong, not only to protect EGFs from the wound hostile environment, but also to allow the GF release in a controlled manner so that dose and administration frequency may be reduced.

Piper sarmentosum Enhances Angiotensin Converting Enzyme 2 Expression in Cultured Human Umbilical Vein Endothelial Cells

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Background: A homologue of angiotensin converting enzyme (ACE) known as ACE2 is mainly expressed in endothelial cells and catalyses the conversion of angiotensin (Ang) II to Ang 1-7. Ang 1-7 is a vasodilator that opposes many of the adverse cardiovascular effects of Ang II, including hypertension. *Piper sarmentosum* (PS) is an herb with antihypertensive activity. Our preliminary data showed that PS reduced ACE and Ang II in human umbilical vein endothelial cells (HUVEC). However, PS effect on ACE2 is still unknown.
Methods: HUVEC were divided into four groups: control, treatment with 200 µg/ml aqueous extract of PS, induction with 200 nM phorbol 12-myristate 13-acetate (PMA) and concomitant treatment with PMA and PS for 24 hours. Subsequently, ACE2 mRNA expression, protein and activity in HUVEC were measured.
Results: As compared to control, induction of HUVEC with PMA caused a decrease in ACE2 mRNA expression ($P<0.05$), protein level ($P<0.05$) and activity ($P<0.05$). Treatment of PMA-induced HUVEC with PS successfully increased ACE2 mRNA expression ($P<0.05$), protein level ($P< 0.05$) and activity ($P< 0.05$).
Conclusion: *Piper sarmentosum* stimulates ACE2 mRNA expression, protein level and activity in PMA-induced HUVEC. This partly explains the herb's antihypertensive mechanisms.

Keywords: Hypertension, Angiotensin converting enzyme 2, phorbol myristate acetate, *Piper sarmentosum*, Human umbilical vein endothelial cells

Expired Human Platelet Concentrate As a Source of Platelet Lysate for the Culturing Skin Dermal Fibroblasts.

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Background: Currently, foetal bovine serum (FBS) is used for *in vitro* cell culture to support cell survival and proliferation. However, the use of FBS for the culturing of cells intended for clinical application should be avoided to minimise the risk of animal pathogen transmission and immunology reactions in the transplanted host. As the alternative, chemically-defined medium and human derived supplement such as human serum and human platelet lysate (hPL) can be used for the expansion of clinical grade cells. As chemically-defined medium is very expensive, thus, the use of hPL is considered a better choice. In this study, we examine the hPL prepared from expired platelet concentrates via repeated freeze-thaw cycle and centrifugation.

Methods: Human fibroblasts were seeded at 3000 cells/cm^2 in 6-well plate with medium DMEM/F12 supplemented with 5% hPL, 10% hPL and 10% FBS. The cell morphology, yield, viability, proliferation rate, extracellular matrix (ECM) gene expression and wound healing were recorded. The gene expression of ECM proteins, i.e. type I collagen (Col I), type III collagen (Col III) and fibronection (FN), were measured via RT-PCR. Wound healing was determined via scratch wound assay.

Results: Fibroblasts of all groups showed viability above 90%. Morphologically, fibroblasts cultured with hPL were more spindle in shape and smaller in size. Cell yield and proliferation rate were significantly higher in the 10% hPL group compared to other groups. However, fibroblasts cultured with hPL have significantly lower gene expression of the ECM proteins compared to those cultured with FBS. Fibroblasts cultured with hPL failed to close the scratch wound after 9 days whereas fibroblasts cultured with FBS only took 3 days to be fully recovered.

Conclusion: Culturing fibroblasts with hPL can shorten the culture period, thus, reducing the cost, time and effort needed.

Keywords: Platelet concentrate, human platelet lysate, fibroblast, wound healing

Kelulut Honey Improves the Memory of the Metabolic Syndrome-Induced Rats

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Background: There are mounting evidence that implicates the pernicious effects of Metabolic Syndrome (MetS) with neurological deficits. Understanding the pathophysiology of MetS is paramount to halt its progression that leads to brain disorder. Supplementary intervention is still lacking due to scarcity of support from scientific evident. Such example is honey which possesses antioxidant that shows potential in protecting the brain. Kelulut honey (KH) which derived from Stingless bee has more phenolic content, a potent antioxidant, than other types of honey. The aim of this study is to determine the effects of KH on anxiety and memory of the MetS-induced rats.
Methods: Twenty-four Wistar male rats were divided into 3 groups; Control (C16) group, high fat high fructose (HCHF) diet (MetS16) group and HCHF diet supplemented with KH (KH) group. The HCHF diet was given for 16-weeks. Fasting blood glucose, lipid profile and blood pressure were then measured, followed by open field and Morris water maze tests.
Results: The HCHF diet induced four out of five risk factors of MetS; high systolic blood pressure, abnormal fasting serum glucose, elevated triglyceride (TG) and reduced high density lipoprotein which confirmed the diagnosis of MetS. Supplementation of KH improve some of these parameters. It reduces fasting blood glucose level ($p<0.05$) compared to MetS16 group. Total cholesterol and low density lipoprotein levels were also significantly reduced ($p<0.05$) compared to the C16 group. It also lowers the systolic blood pressure ($p<0.05$) compared to MetS16 group. KH group showed less anxious behaviour than MetS16 group as demonstrated by higher percentage of time spent in the centre of the arena. Probe trial of Morris water maze showed significant increase ($p<0.05$) in time and distance percentage in the target quadrant in KH group than MetS16 group.
Conclusion: KH supplementation was shown to improve fasting blood glucose, reduces TG level while helps to maintain a normal blood pressure. KH group also showed less anxious behaviour and intact spatial memory compared to MetS group. Kelulut honey may be a beneficial supplementation in patient with MetS especially during its early phase.

Keywords: Metabolic syndrome, kelulut honey, Morris water maze, open field

Ginger Extract Improves Cell Viability and Prevents Cellular Ageing of Human Myoblasts in Culture

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Introduction: Sarcopenia is characterized by loss of muscle mass and function, which occurs with increasing age, with risk of physical disability, poor quality of life, and death. In addition to the existing oxidative stress during ageing, insufficient antioxidant intake contributes to the occurrence of sarcopenia. Ginger or *Zingiber officinale Roscoe Zingiberaceae* contains many phenolic compounds such as gingerol, shogaol and paradol that exhibit antioxidant, anti- tumor and anti-inflammatory properties suggesting that it could be useful in sarcopenia prevention.
Objective: This study aimed to determine the effects of *Zingiber officinale* extract on the viability and senescence biomarker expression of human myoblast cells in culture.
Methods: Young and senescent myoblast cells were treated with series of concentration of two types of *Zingiber officinale* extract (6-gingerol-rich and 6-shogaol-rich extracts) ranging from 10 µg/mL to 1000 µg/mL. Two dosages these extracts were then selected for senescence-associated β-galactosidase (SA β-Gal) assay.
Results: Treatment of 6-gingerol-rich and 6-shogaol-rich ginger extracts were able to increase cells viability of young myoblasts from concentration of 20 µg/mL and not toxic to the cells up to concentration of 1000 µg/mL significantly ($p<0.05$). Meanwhile, for senescent myoblasts, the dosage of both extracts were able to increase cells viability from 100 µg/mL and also not toxic to the cells up to concentration of 1000 µg/mL. Two dosages of 50 µg/mL, 200 µg/mL and 100 µg/mL, 300 µg/mL 6-gingerol-rich ginger extract were used to treat young and senescent myoblasts respectively in the subsequent experiment. Treatment of 50 µg/mL and 200 µg/mL 6-gingerol-rich ginger extract did not cause any significant change on SA β-Gal expression in young myoblasts. However, treatment of 100 µg/mL and 300 µg/mL 6-gingerol- ich ginger extract to senescent myoblast reduced significantly ($p<0.05$) the number of cells positive to SA β-gal staining. In addition, treatment of 6-gingerol-rich ginger extract to senescent myoblast resulted in similar

morphological structure of young myoblast cells.
Conclusion: Treatment of ginger extract increased the viability of myoblast cells and reduced the percentage of senescent cells positive to senescence biomarker indicating its potential in preventing cellular ageing or cellular senescence of human myoblasts, which is beneficial for the prevention of sarcopenia.

Keywords: Ginger extract, myoblasts, cell viability, senescence biomarker, sarcopenia

Health ID – The Key to Trust A Trustless System in Healthcare

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Medical Record Data sharing has been plagued with privacy concerns. A Self Sovereign Health ID built on trustless Distibuted Ledger Technology (DLT) can be an effective proposition in providing privacy, authenticity and security of medical data. The Health ID enables medical record exchange between hospitals with confidence that patient data privacy and security are not compromised. It has the potential to empower patients to decide whom has access to their medical data or contribute their medical data for research purpose. Healthcare and research institutions likewise can trust the data which are signed and authenticated with cryptography.

Loss of Bacterial Diversity and Poor Fibre Intake in Women with Previous History of Gestational Diabetes: Are Probiotics the Answer for It?

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Background: Women with previous history of gestational diabetes (GDM) have a seven-fold increased risk for future diabetes. Pharmacologic approach and dietary intervention are ineffective in reversing pre-diabetic condition. We aimed to investigate gut microbiota composition, glucose homeostasis and dietary intake of post GDM women.

Methods: Socio-demographic data, obstetric history and anthropometrics of women with previous GDM were attained through delivery record from September 2017 to June 2018. Dietary records were obtained via a 3-day dietary recall and analysed through computerized analysis program. Blood was sent to assess glycaemic control. To assess gut microbiome, faecal samples were sent for 16S sequencing. Probiotics intervention was commenced after baseline measurement for 12 weeks.

Results: Women were grouped into impaired glucose tolerance (IGT) (n=11) and normal glucose (n=6). 63.6% of IGT have family history of type 2 DM, required insulin during pregnancy and high postpartum BMI. The average daily calorie intake and macronutrient within normal limit. However, the daily fibre intake was below recommendation. Baseline glycemic control for both groups was normal. Gut composition of IGT women was dominated by *Bacteroidetes* with a small proportion consisted of *Firmicutes, Verrucomicrobia*, and *Proteobacteria*.

Conclusion: Post GDM women with impaired glucose were obese and deficient in dietary fibres have gut microbiome composition comparable as type 2 DM patient. Restoring intestinal homeostasis using probiotics is a promising strategy in reversing pre-diabetic state.

Druggable genes for Malays Familial Hypercholesterolemia (FH) Patients: Insights from Whole Exome Sequencing (WES)

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Background: Familial hypercholesterolemia (FH) is an autosomal dominant disease involving lipid metabolism. Mutations in the *LDLR*, *LDLRAP1*, *APOB*, and *PCSK9* genes have been identified in FH. Here, we performed whole exome sequencing (WES) and examined potential druggable genes associated with Malay FH patients.
Methods: FH patients (n=25) were classified into possible or definite FH based on the Simon Broome's criteria. Single-end whole exome sequencing at 150 cycles was performed on the Ion Proton. Torrent Suite software was used for quality assessment, coverage analysis, alignment and variant calling. Annotation was performed using wAnnovar, and prioritization was accomplished using Phenolyzer. The druggability of the genes was assessed using multiple databases including DGIDB, PharmGKB, Therapeutic Target Database, DrugBank and Pharos. Statistical significance, when appropriate, was performed using GraphPad Prism v7.0.
Results: High low density lipoprotein (HLDL) individuals have significantly more alterations in hypercholesterolemia-related genes compared to low LDL (LLDL) group. *LDLR, APOB, ABCG5, ABCG8* and *PCSK9* genes with Phenolyzer score of more than 0.75 suggesting that these genes are involved in certain phenotypes. Three variants in the *LDLR* gene (rs688, rs2738466 and rs5925) and two variants in the APOB gene (rs1367177 and rs676210) were druggable targets.
Conclusion: Identification of druggable genes involved in FH is important for precision and personalized treatment. Through WES, the first tier gene mutations (*LDLR*, *LDLRAP1*, *APOB*, and *PCSK9*) causing FH as well as the druggable genes can be identified. We have identified 5 druggable targets in the *LDLR* and *APOB* genes, thus precision and personalized approach should be used to treat FH patients with these mutations.

Keywords: Druggable genes, Familial Hypercholesterolemia (FH), Whole Exome Sequencing (WES)

Digital Signal Processing and Fuzzy Clustering for Vascular Compliance and Classification Compliance

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Background: Cardiovascular disease (CVD) is one of the diseases that result in deaths of 17.7 million people annually, this is 31% of all global deaths. High hypertension, diabetes and lipids are the most important CVD risk factors. The challenge for preventing cardiovascular risk factors is closely related to current lifestyles and costs involved in the practice of current medical prevention. In this project, a simple technique of using smartphone applications has been introduced in heart rate monitoring based on cluster techniques.
Methods: The prototype methodology has been used in developing the proposed solution. There are 3 phases of development: application development, development of processing algorithms followed by the test phase. This mobile application consists of registration, data retrieval and processing (DCP) modules, and reporting. Registration modules including demographic registrations and clinical data, the DCP module consists of streaming video and K-Means algorithm development for distribution. Furthermore, the reporting module displays the heartbeat rate generated and its position in the built group. In this project, the human finger tip biomechanical touch and advantage has been utilized through high-performance camera sensors with highly sensitive sensing structures.
Results: The data processing and results of the data sets prove the performance of sensors that can extract an accurate and reliable heart rate non-invasive. This app can produce an easy technique for monitoring heart rate consistency and its position in the normal range.
Conclusion: Overall, this project demonstrates that mobile phone cameras as sensors can be used in self health monitoring and can be expanded to be used in metabolic control and non-threatened blood circulatory system in the future.

Keywords: Digital Signal Processing, Fuzzy Clustering, Vascular Compliance, Vascular Classification Compliance

A Capacitive Electromyography Sensor for Extramural monitoring of Muscle Activity

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An important biosignal often used in clinical diagnosis, medical treatment, and rehabilitation for patients with musculoskeletal disorders is electromyography (EMG). Conventional EMG measurements are done using contact electrodes such as needle electrode (nEMG) and surface electrode (sEMG) that require the attention of a professional medical officer throughout the tedious skin preparation and complex measurement process, limiting the efficiency of the EMG measurement and portability of the system. Recent technological developments in amplifier electronics allow the use of small capacitive EMG (cEMG) biosensor. These electrodes can measure the EMG signals without galvanic contact with the human body which overcome the limitations of the contact electrode. We are developing a cEMG biosensor that can be applied to an ambulatory monitoring system of muscle activity. The main components of the measurement system are the capacitive electrode, front-end amplifiers, pre-processing filters, a data acquisition unit, and the user interface for data storage, analysis, and monitoring. An electrical model of skin- electrode capacitance was developed and derived to determine the optimum capacitance for a cEMG biosensor. Experimental results showed that the cEMG biosensor was able to measure EMG signal accurately and achieved extremely low noise floor of less than 2 mV. This cEMG biosensor was also able to measure the EMG signal with fabric as an insulator. This cEMG biosensor was able to overcome the limitations of the contact electrodes, yielding a comparable performance to EMG signals measured by conventional wet contact electrodes which makes it ideal for ambulatory applications.

Effect of Naringin on Osteoporosis and their Mechanism of Action: Review

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Background: Osteoporosis is a 'silent killer' marked by reduced of bone minerals, leading to an increased risk of bone becoming fragile and fractured even with a small fall. Studies have shown that plant based therapy have a potential strategy for the management of osteoporosis because of their promising role in enchancing bone density and mass. Naringin is a type of flavonoid compound found in citrus fruits and grape fruits have showed a tremendous effect on bone metabolism.
Objective: This review paper was aimed to study the effect of naringin on bone remodelling and prior with osteoporosis.
Methods: A literature research was done on the effects of naringin on osteoporosis using the Ovid Medline, Ebsco Host and Scopus databases. Specific descriptors were used to perform the search strategy. The article were selected based on the principle that reports on the effect of naringin on treating osteoporosis.
Results: A total of 311 articles were screened from three of the electronic databases, based on the inclusion and exclusion criteria. From the strategy research a total of 10 articles were selected, 3 from Ovid Medline, 5 from Ebsco Host and 2 from Scopus. Based on the chosen article, naringin exhibit its ability to improve the bone generation factors and overcome the bone demineralizing activity.
Conclusion: This review demonstrate that naringin offer a potential in the management of osteoporosis by increasing the proliferation of new bone cell and inhibiting resorption activities.

Keywords: Naringin, flavonoids, osteoporosis, bone resorption, bone formation

Wharton Jelly Stem Cells Culture for Mass production Expansion using Good Manufacturing Practice-Compliant Media Optimization

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Background: Mesenchymal stem cells (MSCs) has been described as multipotent progenitor cells that are capable to differentiate into various type of cells such as osteoblasts, chondrocytes, and adipocytes. Wharton jelly is a rich source of mesenchymal stem cells and has been proven to be more proliferative, immunosuppressive and therapeutically active than other sources of MSCs such as bone marrow and fat. Furthermore, umbilical cord where there Wharton jelly resides are redundant tissues often discarded after birth thus making MSCs from Wharton jelly the perfect candidate for allogenic cell-based therapy. This study was conducted to identify the ideal media to be used as part of the strategy for mass culture expansion of human Wharton jelly derived mesenchymal stem cells (hWJ-MSC) in vitro according to GMP standards. A range of media that were available commercially was tested. Ideally the media should be defined, free of animal product and is of GMP-grade. This optimization is important before the strategy can be employed to achieve economy of scale in the development of a commercially viable therapeutic product.

Methods: The umbilical cord tissue that consists of Wharton jelly component was shredded into small pieces and was enzymatically digested using 0.6% of collagenase type 1 for 1-2 hours at 37˚C. The isolated cells were separated into 7 groups and cultured in four different commercial culture media, i.e. i) DMEM (low glucose) supplemented with 10%FBS (DMEM-FBS), ii) DMEM (low glucose) supplemented with 10% human platelet lysate (DMEM-HPL), iii) MSC-specific defined media (MSC-DM1), iv) MSC-specific media supplemented with human platelet lysate (MSC-HPL), v) MSC-DM2, vi) MSC-DM3 and vii) GMP-grade MSC-DM4. Cell morphology, cell attachment rate, population proliferation rate and doubling time were then analysed. The optimal media was then used for the mass expansion of hWJ-MSCs.

Results: Cells grown in MSC-DM2, MSC-DM3, GMP-grade MSC-DM4 did not

attach at P0 and were discarded. The attached hWJ-MSCs (in group i-iv) resumed a fibroblast-like morphology and those in DMEM-FBS were significantly larger compared to those in other groups. However, cell attachment rate was not significant different across these groups ($p>0.05$). At passage 2 (P2), cell proliferation rate for MSC- HPL group was significantly higher compared to other groups (DMEM-FBS: $5 \pm 1 \times 10^4$ day^{-1}; DMEM-HPL: $2 \pm 1 \times 10^4$ day^{-1}; MSC-DM: $7 \pm 5 \times 10^4$ day^{-1}; MSC-HPL: $26 \pm 3 \times 10^4$ day^{-1}). Cell yield at P2 was also significantly higher for MSC-HPL group compared to other groups ($p \leq 0.0005$). Our preliminary attempt using MSC-HPL, successfully produced 100 million hWJ-MSCs in 29 days from a 6cm length umbilical cord with a cell viability of 94%.

Conclusion: It was concluded that MSC-HPL is superior to other culture media for hWJ-MSC in vitro expansion and can be successfully used for hWJ-MSC mass expansion. This media is however not defined due to the supplementation of human platelet lysate and it is of R&D grade. Hence, further risk assessment will need to be performed and subsequent study is required to validate the therapeutic properties of cells expanded using MSC-HPL before introduction into GMP manufacturing.

Keywords: Stem cells, Wharton jelly, mass production expansion, GMP compliant

Acknowledgement: This work was supported by Universiti Kebangsaan Malaysia, under University Research Grant AP-2017-009/2.

Influence of *MIR499* rs3746444 Polymorphism on Breast Cancer Susceptibility: A Meta-Analysis

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Background: MicroRNA-499, encoded by the *MIR499* gene, plays important regulatory roles in many breast cancer-related pathways. Polymorphisms within the *MIR499* gene could potentially influence the function of the microRNA, which could in turn, affect breast cancer susceptibility. A number of genetic epidemiological studies have investigated the relationship between *MIR499* rs3746444 polymorphism and breast cancer susceptibility, but the results obtained have been inconsistent. This meta-analysis was conducted to better evaluate the association of the polymorphism with breast cancer susceptibility.
Methods: Literature search was conducted using PubMed, Web of Science and Scopus databases up to October 2018. Eligible studies which fulfilled specific inclusion and exclusion criteria were selected and the relevant data was extracted. Odds ratio (ORs) and 95% CIs were then determined separately for five genetic models: homozygous (GG vs. AA), heterozygous (AG vs. AA), dominant (AG+GG vs. AA), recessive (GG vs. AA+AG) and allele contrast (G vs. A).
Results: A total of 10 studies (comprising 4,376 cases and 5,050 controls) were included in the meta-analysis. The pooled ORs showed that the *MIR499* rs3746444 polymorphism was significantly associated with increased breast cancer susceptibility under all genetic models (homozygous, OR=1.46, 95% CI=1.24–1.71, $P<0.001$; heterozygous ,OR=1.11, 95% CI=1.01–1.21, $P=0.020$; dominant, OR=1.15, 95% CI=1.06–1.25, $P<0.001$; recessive, OR=1.32, 95% CI=1.03–1.68, $P=0.030$; allele contrast, OR=1.16, 95% CI=1.04–1.29, $P=0.006$).
Conclusion: The present meta-analysis provides statistical evidence that the *MIR499* rs3746444 polymorphism could contribute to increased breast cancer susceptibility. However, future studies with larger sample sizes are warranted to confirm and strengthen this finding.

Keywords: Breast neoplasms, genetic association, genetic variation, microRNA, risk

Detection and Confirmation of the Presence of Long Non-coding RNA in Archival Frozen Whole Urine Samples

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Background: Urinary RNA detection represents an ideal and non-invasive platform for biomarker discovery in urologic disorders. However, no standardized method of RNA detection for urine samples has been established, particularly in detecting the long non-coding RNA (lncRNA) expression. Moreover, urinary RNA yields and quality were shown not to be consistent in previous publications. Here, we aimed to determine the optimum method of extracting and detecting the lncRNA expression in archival frozen whole urine samples.
Methods: We used a systematic evaluation of the best RNA extraction methods and cDNA synthesis methods to detect the presence of lncRNA. Briefly, whole urine samples, which have been frozen for one month, from the healthy volunteers, were extracted with two different methods of RNA extraction, a Trizol-phenol and a commercial kit. All RNA samples were assessed for their purity, concentration and integrity. Following this, the samples were subjected to cDNA synthesis methods either with pre-amplification step or not. Expression of *U6* (housekeeper circulating gene), miR-21 (a well-known microRNA in urine) and *MALAT-1* (a selected lncRNA) were measured using SYBR qPCR.
Results: The RNA yield from the commercial kit was better than the Trizol-phenol method, with a range of 400ng to 1000ng of RNAs from a total of 400µl of urine. Though, both RNA extraction methods gave lower purity readings despite having reasonable RNA concentrations. Expression of *U6* and miR-21 were detected in all samples, regardless of the RNA extraction and cDNA synthesis methods. However, expression of MALAT-1 was only consistently present in the RNA samples that went for the pre- amplification step during cDNA synthesis.
Conclusion: We have successfully validated the method for lncRNA detection in frozen whole urine samples. We showed that MALAT-1 is present in the urine samples of healthy volunteers. However, it is recommended to do a pre-amplification step before the gene expression analysis, in order to detect this lncRNA in the urine samples.

Keywords: RNA detection, method optimisation, long non-coding RNA, urine samples

Investigating Potential Role Of 5-HT3 Receptor Antagonists In Modulating Nicotine Rewarding Effect Using Conditioned Place Preference

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Background: The 5-HT3 serotonin receptor (5-HT3R) is a ligand-gated cation channel which belongs to the same family of nicotinic acetycholine receptor. It is currently a clinical target for nausea and vomiting the use of 5-HT3R antagonists. It has also been reported to have important roles in mental related disorders including drug abuse, by regulating the release of dopamine, a major event which underlies drug addiction. The aim of this study is to explore the potential role of 5-HT3 antagonists in modulating nicotine addiction in view of seeking for an alternative target for smoking cessation treatment.
Methods: Nicotine-induced rewarding effect in mice was studied by using conditioned place preference (CPP) method. Alleviation of the rewarding effect was investigated using ondansetron, palonosetron, 6-gingerol and 6-shogaol which are all 5-HT3R antagonists. 90 Swiss Albino mice were randomly divided into 15 groups (saline control, nicotine control, bupropion as positive control, ondansetron (0.5, 1.0 and 2.0 mg/kg), palonosetron (10, 30 and 60 mg/kg), 6-gingerol and 6-shogaol (both with doses on 70, 100 and 130 mg/kg)). All mice were given saline and 1.0 mg/kg of nicotine s.c. on alternate days and were subjected to first phase (conditioning) of CPP to induce nicotine addiction. Following confirmation of nicotine-induced addiction, 5-HT3 antagonists were administered 15 minutes prior to administration of 1.0mg/kg nicotine and were subjected to conditioning phase again. CPP test was conducted in three phases, which were pre-conditioning, conditioning and post- conditioning. The time spent in each compartment was recorded and calculated. Percentage preference towards drug-paired compartment during post-conditioning phase was analysed using one-way analysis of variance (ANOVA) followed by Tukey's test.
Results: Significant reduction of nicotine rewarding effect was observed following administration of 1.0 mg/kg of ondansetron, 60 mg/kg of palonosetron, 130 mg/kg of 6- gingerol and 100 mg/kg of 6-shogaol.
Conclusion: The effects observed demonstrated that ondansetron, palonosetron,6-gingerol and 6-shogaol have potential in reducing the rewarding effect of nicotine in mice.

Keywords: Nicotine addiction, 5HT3 antagonist, Ondansetron, Palonosetron, 6-gingerol, 6- shogaol

The Prospect of Cell Therapy for Treating Aging-associated and Degenerative Diseases

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The natural process of aging is accompanied by the process of degeneration in the organ, tissue and cells. This process ultimately stems from changes at the chromosomal and epigenetic levels as DNA undergoes replication and pressure from external stimuli. The possible solution to this can act on trying to reverse changes at any of the levels and one such possibility is to reverse these changes at the molecular level or to replace the aging cells with new ones. The proposal to use cell therapy to reverse the effects of aging is hence a very logical one. With the advent of stem cells which have the ability to proliferate extensively and differentiate into many cell types in the body, the prospect of cell therapy is even more promising. The mechanisms by which these cells work on are beginning to shed light on the how future therapies can be designed. A study on efficacy and mechanism of action of mesenchymal derived stem cells in treating diet-induced metabolic syndromes have also been initiated with the support from the industry and University Research Grant AP-2017-009/2.

Fibroblasts Secreted Proteins Promote Skin Regeneration *in vitro* and *in vivo*

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Background: Severe skin injury affects the patient's quality of life even death if healing progress is delayed. Wound healing mediators such as cytokines, chemokines, growth factors and extracellular matrix (ECM), which is secreted by fibroblasts in native tissue, are required for regeneration of skin tissue. These secreted proteins can be collected by culturing fibroblasts *in vitro* as dermal fibroblasts conditioned medium (DFCM). The study aimed to collect the DFCM and investigated the composition and effect of DFCM on skin regeneration *in vitro* and *in vivo*.

Methods: Human skin samples were collected with the patient's consent and used to isolate skin cells, i.e. fibroblasts and keratinocytes. Fibroblasts were cultured until confluence and incubated with serum-free culture medium to collect secreted proteins. Analysis of the protein composition was performed via 1D-SDS-PAGE and mass spectrometry. Regeneration potential of skin cells *in vitro* was evaluated using the cellular attachment, proliferation and migration. Moreover, an acellular 3D skin patch was fabricated using collagen hydrogel fortified with DFCM. The skin patch was implanted on the skin injury mice model to evaluate the healing efficiency.

Results: Proteomic analysis demonstrated that the concentration and composition of proteins in DFCM depends on the culture duration, passage number and medium. Secretory proteins in DFCM include growth factors, cytokines, chemokines and ECM. The bioinformatic analysis revealed the involvement of these proteins in skin wound healing. Also, supplementation of DFCM *in vitro* promotes the skin cells proliferation and migration. Implantation of a skin patch with or without DFCM in an animal model demonstrated significantly faster healing compared to control after 7 days. The histological analysis shows the intact epidermis layer in the test group.

Conclusion: Presence of wound healing mediators in DFCM facilitates the regeneration of skin both *in vitro* and *in vivo* and potential to be used as skin

substitutes for the treatment of skin injury.

Keywords: Regeneration, Skin, Fibroblasts, Conditioned Medium, Wound Healing

Healthcare Facilities Management: a Proposal for Asset Information System at Women and Children Hospital Kuala Lumpur

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Background: Konsortium ProHawk Sdn Bhd (KPSB) has been awarded the contract for the establishment of a management information system at Women and Children Hospital Kuala Lumpur (WACH) which is a new hospital developed using private fund initiative (PFI). This paper describes the implementation of the WACH Asset Information System (WAIS) for managing and tracking the performance of facilities management (FM) at WACH.
Methods: WACH Asset Information System is owned by KPSB's service provider, Edgenta Healthcare Management Sdn Bhd (EHMSB) that is currently the concession company responsible to develop WAIS. The first version of the system named as WAIS 1.0 mainly contains the details of asset registration storage for asset tracking system (ATS) using management information system (MIS) called Eclip and system integration.
Results: In WAIS 1.0, the engineering modules such Facilities Engineering Maintenance Services (FEMS) and Biomedical Engineering Maintenance Services (BEMS) are automated whereas the hygiene modules are fully manual. Due to lack of automation and further requirement by the Ministry of Health (MOH), WAIS 2.0 has been proposed to suit with both MOH and WACH's requirements on few contractual criteria and targeted at being able to cater for 27 years of service. In line with the current trend of internet of thing, WAIS 2.0 will be upgraded to mobile application and will cater the operation using Android operating systems.
Conclusion: Further improvement adopted in WAIS 2.0.is expected to eradicate complications and difficulties of WAIS 1.0 as in the new performance monitoring will be made possible. This improvement is not only for WACH but also other hospitals which are about to develop niche asset information systems for their support services.

Keywords: Facility management, performance monitoring, information system

Nutritional and Bone Health Status in Young Men with and without Intellectual Disability (ID) in Malaysia

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Background: Studies on bone health status among people with intellectual disability (ID) are limited despite this population was found to have poor nutritional status which could potentially influence bone health status compared to the general population. This study aimed to compare the nutritional status and bone health status and to quantify the association between bone health status and its determinants among young men with and without ID in the central region of Malaysia.
Methods: This cross-sectional comparative study was carried out in 95 men (47 mild to moderate ID; 48 without ID), aged 20-39 years. Data collected include sociodemographic profile, anthropometric status, dietary intake and physical activity level. Bone health status was determined by calcaneal speed of sound (SOS) using qualitative ultrasound device.
Results: Malnutrition incidents (underweight and obese) and body fat percentage were higher in ID participants compared to men without ID ($p=0.037$; $p<0.001$). The ID men had moderate diet quality (healthy eating index (HEI) score = 53.6) compared to poor diet quality among men without ID (HEI score = 39.7; $p<0.001$). Both mean dietary calcium intakes among ID (373 mg/day) and without ID (369 mg/day) did not reach the recommended intake (1000 mg/day). Majority ID participants (97.9%) were found to be less active than their counterparts (10.4%; $p<0.001$). The mean SOS value showed no difference between group ($p>0.05$) and were lower than the Malaysian reference ($p<0.001$). No relationship was observed between bone health status and bone determinants within ID participants. Height and body fat mass were negatively associated with SOS among the typical men ($p<0.05$).
Conclusion: Both young men with and without ID in Malaysia have suboptimal nutritional status and low bone health status. Future research on nutritional intervention program, specifically aiming to improve nutritional and bone health status for men in Malaysia is warranted.

Keywords: Intellectual disability, diet quality, nutritional status, bone health, quantitative ultrasound

Constructs Formed with G Protein Intercalated Human Mesenchymal Stem Cells on Gelatin Microsphere Promotes Cell Proliferation, Stemness and Differentiation Potential

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Background: Translation of stem cell-based therapies to clinical trial requires viable delivery vehicles that can regulate stem cell behaviour. Even though regulated, the engraftment and low homing of the injected mesenchymal stem cells (MSC) to specific damage tissue continues to be a problem. Thus, the suitability of gelatin microspheres (GM) as such a tissue engineering platform and optimizing cell membrane glyco-engineering can address this limitation.
Methods: Gelatin was dehydrothermally crosslinked at 140°C for 48 hr in a water-in-oil emulsion state. MSC from consented patients were cultured on GM and the cell membranes was intercalated with protein G (PPG; 100 µg/ml) followed by incubation with type II collagen antibody solution. Analyses has been performed to assess stem cell properties, proliferation and attachment ability of MSC after the intercalation process. Chondrogenesis potential of intercalated MSC also was evaluated.
Results: Results demonstrate that intercalation process does not affect the growth kinetics of the cells and retained the MSC properties as well. Cultured cells were shown attached and proliferated on the GM comparably to the control (MSC without intercalation process). The cells also positively differentiated into multilineages of the mesoderm i.e. fat, bone and cartilage cells as confirmed with Oil Red O,

Alizarin Red and Toluidine Blue staining respectively. Intercalated MSC revealed a similar pattern of extracellular matrix (ECM) deposition during chondrogenesis comparative to that of positive control.
Conclusion: These results suggested that culturing G-protein intercalated MSCs on GM is a viable method for future target cell delivery without affecting the properties of the cells. It is potentially safe to be applied to any cell or tissue application in the future.

Keywords: Lapidating, stem cells therapy, protein G

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Effect of *Christia vespertilionis* on TNF-α-Induced Pro-Atherogenic Adhesion Molecules Expression in Endothelial Cells

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Background: The expression of cell adhesion molecules by endothelial cells has been identified as one of the early event in pathogenesis of atherosclerosis. *Christia vespertilionis* has been shown to exhibit anti-malarial and anti-cancer properties. This study aimed to investigate the effect of *C. vespertilionis* on tumour necrosis factor (TNF)-α induced expression of pro-atherogenic adhesion molecules in endothelial cells.
Methods: Effect of hydroethanolic extract of *Christia vespertilionis* and the hexane, ethyl acetate, acetone and ethanol fractions on expression of TNF-alpha-induced vascular cell adhesion molecules (VCAM-1) protein expression in human umbilical vein endothelial cells (HUVECs) was determine through Western blotting.
Results: *C. vespertilionis* extract inhibit TNF-α-induced VCAM-1 protein expression in a dose- dependent manner. *C. vespertilionis* extract at concentrations 5, 10 and 20 µg/mL inhibited TNF-α-induced VCAM-1 protein expression at 67.6%, 56.6% and 36.9%, respectively. Among the four sub-fractions of *C. vespertilionis*, ethyl acetate fraction exhibited the highest inhibitory effect on VCAM-1 protein expression. By treatment of 2.5, 5 and 10 µg/mL of EA fraction, the VCAM-1 protein expression were 48.6%, 47.6% and 45.2% compared to negative control.
Conclusion: In conclusion, this study demonstrates that *Christia vespertilionis* extract may inhibit TNF-α-induced VCAM-1 protein expression in HUVEC, suggesting that this plant could be further researched for its beneficial use in inflammatory disorders.

Keywords: *Christia vespertilionis*, vascular cell adhesion molecules, endothelial cells

Alzheimer's Disease - Challenges for Control and Treatment

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Alzheimer's disease (AD) is characterized by a progression from episodic memory problems to a slow global decline in cognitive function. The neuropathological hallmarks are senile plaques, and neurofibrillary tangles. The first genetic mutations causing familiar AD were discovered in the amyloid precursor protein (APP) gene. Thus, the amyloid hypothesis is proposed that the deposition of Aβ is the primary event in AD pathology. However, clinical trials of Aβ-targeting drugs including Aβ vaccines have been failed. Recent evidence shows that the amyloid pathology occurs about twenty years before a clinical onset of AD. When cognitive decline of AD patient occurs, the patient must show massive senile plaques, neurofibrillary tangles and neuronal loss in the brain. Therefore, Aβ-targeting drugs should be applied to very early stage of AD patients such as preclinical and mild cognitive impairments (MCI) stages, in order to prevent dementia (pre-emptive medicine). People with preclinical AD are clinically normal subjects. Therefore, it is important to treat them without any serious side effects. In this point of view, it is of great interest to find therapeutic drugs from natural food products. On February 14th 2014, UKM Medical Center in Universiti Kebangsaan Malaysia (UKM) and Molecular Neuroscience Research Center (MNRC) in Shiga University of Medical Science (SUMS) has agreed collaborative research entitled "Unravelling the transitional events of normal to pathological aging leading to cognitive decline". Since then, we have studied molecular mechanisms of cognitive decline in aging and AD. We have also examined therapeutic effects of compounds from natural food products such as palm-tree derived tocotrienol rich fractions (TRF) and curcumin derivatives using rat and mouse models. Both TRF and curcumin derivatives prevented cognitive decline and reduced amyloid pathology of transgenic mouse models of AD. More recently, our collaborative team revealed brain metabolite profiling of wild-type and transgenic mice treated with and without TRF. The results suggest that the mechanism of this pre-emptive activity may occur via modulation of metabolic pathways dependent on Aβ interaction or independent of Aβ interaction.

Adipose-derived Mesenchymal Stem Cells: Potential for Metabolic Therapeutics

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Adipose tissue is a scalable and readily attainable source of proliferating, multipotent mesenchymal stem cells (MSCs), holding great therapeutic potentials. However, more work is necessary to fully understand properties of adipose-derived MSCs (ASCs) in order to maximize their therapeutic potentials. We are interested in identifying novel biomarkers that predict characteristics of ASC functions. In our studies, we performed various experimental approaches including comprehensive image-based high content screening, whole genome-wide gene expression analyses, metabolomics, stem cell function and differentiation assays. We identified novel cell surface markers, CD10 and CD200, which indicate how well ASCs can differentiate into mature functional adipocytes. In addition, novel pathways of retinoid metabolism and oxidative stress were uncovered. Excessive retinoic acid pathway in visceral fat- derived ASCs resulted in interfering with their adipocyte differentiation capacities, which was reversed by inhibitors of its pathway. It was also found that high oxidative stress associated with ageing or visceral obesity affects ASC's ability for differentiation, proliferation, migration and senescence. Treatment with anti-oxidants was effective in reducing reactive oxygen species and improving these ASC properties. Together we demonstrated that specific cell surface markers and metabolic cascades can serve as prospective markers and/or regulate cellular functions of ASCs, which may be useful for further development of cell therapeutic activities using ASCs and other MSCs.

Low-Frequency Group Exercise Improves the Balance, Functional Strength, and Gait Speed of Chronic Stroke Survivors.

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Background: To achieve optimum benefits, the planning of exercise therapy for post-stroke population should follow established exercise guidelines such as those proposed by the American College of Sports Medicine. However, the recommended exercise guidelines, which emphasize high-frequency exercise at least three to five times per week, may be impractical for most stroke survivors due to multi-factorial reasons. In this study, we assessed the effects of a low-frequency (once per week) group exercise therapy on the balance, functional strength, and gait speed of chronic stroke individuals.

Methods: This was a pre-test post-test experimental study. A total of 44 adults with chronic stroke, mean age 58.68 years (SD) = 10.16), and mean duration of stroke 17.18 months (SD=17.34) participated in a 90-min group exercise, which focused on task- oriented training, organized once a week for 12 weeks. The therapy outcomes were measured at week 13 by an independent assessor with the use of standardized clinical tests.

Results: We observed that the therapy improved the group balance score by 2 units, ($Z = 3.88$, $P < 0.001$), speed of standing up for five times from a sitting position by 4.6 s ($Z = 4.66$, $P < 0.001$), and mean walking speed by 11.83 m/min ($Z = 3.226$, $P < 0.001$). Further analysis of the balance performance showed an increase in the mean score of 7 out of the 14 items of the Berg's Balance Scale, indicating significant balance ability improvement among the stroke survivors.

Conclusion: In conclusion, this study showed that a 12-week once-per-week group exercise therapy effectively improves the physical performance of chronic stroke survivors.

Keywords: Chronic stroke, group exercise therapy, physical functions

Tocotrienol-Rich Fraction of Palm Oil Modulated Brain Proteome Profile and Improved Memory in APP/PS1 Mice

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Background: Alzheimer's disease (AD) is a neurodegenerative disorder, characterized by a gradual impairment in memory. Accumulation of amyloid plaques and tau protein neurofibrillary tangles are the pathological hallmarks of AD. Little is known about the effect of vitamin E on AD. Therefore, this study was carried out to evaluate the effect of tocotrienol-rich fraction (TRF), a mixture of vitamin E analogs derived from palm oil on APP/PS1 transgenic mice, a mouse model of AD.

Methods: APP/PS1 mice were supplemented with TRF orally for 10 months. Locomotor and cognitive functions were assessed by the open field, Morris water maze, and novel object recognition tasks. Proteomics analysis was performed on the mice brain using liquid chromatography tandem mass spectrometry. Immunohistochemistry and thioflavin-S staining were performed to examine the TRF effect on amyloid pathology.

Results: APP/PS1 mice treated with TRF showed improvements in exploratory activity, learning, and memory as assessed by the behavioral tests. Proteomics analysis showed that TRF altered proteins in the APP/PS1 mice in a brain region-specific manner. TRF modulated the expression of amyloid beta (Aβ) protein in hippocampus. Reduction of Aβ deposition was also observed in the APP/PS1 mice brain.

Conclusion: TRF supplementation improved exploratory activity, learning and memory abilities in APP/PS1 mice. Amyloid pathology ameliorated with the treatment of TRF. TRF also potentially exerts its neuroprotective effects in APP/PS1 mice brain by modulating proteins involved in various biochemical pathways.

Keywords: Alzheimer's disease, palm oil, brain, proteomics

Bioengineered Living Bilayer Cornea in ex vivo Wound Abrasion Model

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Background: The use of the animal's eye for the drug irritation test has generated much discontentment in recent years due to animal cruelty and its controversial outcome. Ex-vivo living bioengineered cornea, which is able to functionally simulate the in vivo cornea would be a favourable choice to overcome the above problems. The aim of the study is to evaluate the healing properties of the bioengineered living bilayer cornea using sodium lauryl sulphate as an abrasive agent.
Methods: Corneal epithelial cells (CEC) and corneal fibroblasts from New Zealand White rabbit corneas were culture expanded until passage 1. Bioengineered cornea was reconstructed by using corneal fibroblasts in collagen scaffold as the stroma. The stratified corneal epithelium was layered on top of the corneal stroma. Sodium lauryl sulphate (0.1%, 1%) was applied to the corneal construct to create abrasion model. The healing properties of the bioengineered cornea were evaluated via histological analysis and expression of corneal epithelial healing markers (qRT-PCR) on day 1, day 5 and day 10 post abrasion.
Results: Bioengineered cornea remained viable throughout the test. Histological analysis revealed re-epithelialization was almost complete at day 10 in SLS 0.1% group, but epithelial thinning with vacuolization was observed in SLS 1% group. The expression of healing markers; cytokeratin 3, CD44, connexin 43 was comparable to the stage of post abrasion healing. In SLS 1% group, the expression of the markers was comparable to the non-healing corneal abrasion.
Conclusion: Bioengineered living bilayer cornea remained functionally stable and can be used in ex vivo corneal abrasion model. The response of ex-vivo healing is best demonstrated using SLS 0.1% as the abrasive agent.

Keywords: Bioengineered cornea, ex-vivo wound abrasion model, sodium lauryl sulphate

Epigenome Wide Association Study for Cardiomyopathy in Heart Tissues

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DNA methylation, a key mechanism determining gene expression and phenotypic pattern, has begun to offer much promise as a central player in the development of various metabolic disturbances in recent years. Looking beyond genetics has allowed us to not only identify novel biomarkers, but also improve our understanding of underlying biological pathways and mechanisms. In this talk, I will present findings from our epigenome-wide association study (EWAS) where we investigated methylation differences between healthy and diseased heart tissues.

The Effects of Traditional Chinese Medicine KSLP on Adipose-derived stem cells in Aged Mice

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Aging is considered as a major risk factor for the growth and multilineage differentiation potential of Adipose-derived stem cells (ADSCs). In current study, the effects of an anti-aging tablets (KSLP) on ADSCs derived from aged mice were evaluated in the aspects of cell cycle, apoptosis as well as the adipogenesis and osteogenesis abilities of ADSCs. RNA-Seq technology was applied to define differentially expressed genes (DEGs) for biological informatics analysis. Results showed that with the increasing of donor age, percentage of ADSCs in G0/G1 phase rose, in the meantime, their proliferation index decreased. KSLP decreased cells percentage in G0/G1 phase and improved the proliferation index. There was no obviously difference in apoptosis between the groups. In addition, weaken of adipogenesis and osteogenesis of ADSCs appeared in aging mice. KSLP effectively increased the osteogenesis ability of ADSCs. RNA-Seq results showed that there were a total of 146 DEGs between ADSCs derived from 6-8 weeks and 6-8 months mice, and 175 DEGs between ADSCs derived from 6-8 months mice with or without KSLP treatment. GO and KEGG analyses indicated that KSLP may participate in the negative regulation of apoptosis, protein metabolism and modification, osteoblast differentiation and phagocytosis. In summary, our study provided evidences indicating that KSLP can promote the cell proliferation and osteogenesis ability of aged ADSCs, the role of which is related to the negative regulation process of apoptosis, protein metabolism and modification, osteogenesis differentiation and phagocytosis.

Keywords: Aging; ADSCs; Cell cycle; Osteogenesis; RNA-Seq

The Foot Attack

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Wounds are becoming a major problem nowadays especially with the increase in the incidence of Diabetes Mellitus. Diabetic foot is a major complication and the last study by the International Working Group on Diabetic Foot in 2011 found that a foot was being amputated every 20 seconds in the world. Therefore, this has been defined as a foot attack. Therefore, we need new modalities as well as new techniques to manage the cases and prevent limb amputation. Limb salvage is of paramount importance. In Malaysia, the incidence of Diabetes Mellitus is 17.5% from birth and 20% for those above 18 years of age. This epidemic is quite alarming. The National Committee on Wound Care comprising various consultants from various disciplines was formed in 2009 and training was started at all specialist hospitals in the country. Training by zones were initiated. The primary care also followed closely the footsteps of the medical division and Family Medicine Specialists as well as paramedics are being trained. Foot assessments are stressed. Proper footwear and offloading is crucial. Education and workshops for the health care professionals and the patients are done extensively in a coordinated approach. Multidisciplinary team approach is stressed. Various modalities used will be showcased for wound management in handling the foot attack.

The Use of Biologics in Inflammatory Bowel Disease: What Clinicians and Scientists Should Know?

ABBVIE SDN BHD

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Biologics are large complex molecules produced in living systems. They have revolutionised the treatment of patients suffering from various immune-mediated diseases, including inflammatory bowel disease (IBD). IBD is a chronic, relapsing and remitting intestinal disorders and can be broadly classified as either Crohn's disease or ulcerative colitis. The aetio-pathogenesis of IBD is still unknown but interaction of immune dysfunction along with genetic factors, environmental exposure and gut microbiome is thought to be heavily involved in this complex disorders. Its occurrence is steadily increased in particular in the Asia pacific region. However, knowledge, attitude and practice of using biologics for the therapy of IBD is still limited due to many factors which includes lacking of 'cross-talk' between clinicians and scientists. This presentation will discuss about the clinical and scientific issues of IBD through a case study as well as molecular aspect of IBD focusing on the use of biologics as the emerging and effective therapy for IBD.

How Innovations are Transforming Non-Communicable Diseases Prevention and Control

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Public health in the Malaysia has always played a fundamental role in the maintenance and improvement of quality of life of all Malaysians and remains the same today. However, the epidemiological transition of an aging population, increasing burden of Non-Communicable Diseases (NCDs) and health being perceived as low priority by the general population are issues that need to be addressed right now. There is a dire need to address these various public health issues in an integrated manner. Specifically in addressing the increasing burden of NCDs, scientific evidence has shown that NCDs are preventable by addressing the major behavioural risk-factors. However, the challenge has always been making these necessary behavioural modifications happen, and to be sustainable. In Malaysia, current behavioural interventions are not able to deliver effective clinical outcomes that are sustainable in a wide-scale manner. Raising knowledge and awareness by themselves is insufficient to catalyse lasting positive behavioural changes. For promoting healthy behaviours, IT related solutions are appealing because they are empowering to the individual users and can drive behavioural change. Cost saving is also a big driver because these solutions can be relatively inexpensive and scalable when compared to other solutions. In addition, once an idea is developed, it can be rolled out to massive audiences with relative ease. Malaysia has already begun this journey, working together with the private sector and academia.

NCDs: Global trends and challenges for control

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Selangor is the highly developed state with the population of 6016900, changes in life style caused major threat and heavy burden on major non-communicable disease in Malaysia. Therefore diabetes, hypertension and heart disease, cancers, injuries and mental health problem become more and more prevalent. National Health Morbidity Survey (NHMS 2015) reported that 15.5% prevalence of Diabetes in Selangor with higher prevalence among Indians 24.8%, Chinese 19.2% and Malays 54.9%. Out of this only 176420 Registered at Primary Health Clinic. 65.6% of them are from 45 year-65 year of age. Diabetes control by HbA1c <6.5% is only 25.5% for 2018. Many factors contribute to the poor control, these include the ignorance of the community the importance on diabetic care and the managing of diabetes as a whole. From the NHMS also reported 40-60% of our population did not aware they have a risk of either getting diabetes, or hypertension or having high cholestrol that need for further care. With KOSPEN (Komuniti Sihat Pembina Negara), a programmed targetted to the community at large and empowered them to get an early screening. To date Selangor have 253 localities (2017), 40.2% already screened. From 166929, 22917 (34.2%) found to have high blood glucose, hypertension 20048 (29.9%), 7858 (11.7%) BMI >30.0 and 8441 (12.6%) are smokers of which 4742 (56.5%) went for quit smoking clinic. Cancer reported 25343 till Feb, 2018, with10117 (39.9%) death. Breast cancer top the list with 24.3% followed by colorectal cancer 11.3%, lungs 6.4%, leukemia and blood cancers 5.6% and lymphoma 5.3%. By ethnic, the prevalent are among the Chinese with 39.0%, Malay 45.0% and Indian 15.0%. National Institute Cancer of Registery have upgraded their registery from CanReg 4 to CanReg 5 to strengthened and update the registery. 28557 people have screened using DASS in 2017, it was found that 4641 (16.3%) anxiety, 3167 (11.1%) stress and 2434 (8.3%) depression. Whereas 336 new cases reported at Primary Health Clinic with depression hit the list with 158 (47.0%), anxiety 73 (21.7%) and schizophrenia 65 (19.3%). All of non-communicable disease largely contributed by modernization and poor practice healthy life style including healthy eating and not regularly exercise. Therefore, health promotion need to be addressed at all level and at early age.

Molecular Autopsy of Sudden Cardiac Death

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Background: Sudden death due to a heart attack (also referred to as sudden cardiac death; SCD) is not uncommon. The Malaysian Cohort project which has recruited more than 130,000 participants has more than 300 participants who have died of SCD over the follow-up period. Interestingly, over 100 of them had never experienced any prior symptoms. This study aims to investigate the profiles of gene variants in Malaysian patients with SCD.
Methods: Thirty six youngest participants who have died of SCD and 36 age and gender-matched controls were included in this study. The DNA were extracted using NucleoSpin® Blood from 200 µl of blood preserved in EDTA. Libraries were prepared using TruSight® Cardio Sequencing Kit which includes 174 genes with known associations to 17 different cardiac conditions. Pooled libraries were sequenced on the MiSeq sequencers using paired-end, 150 bp reads. The high-quality reads were aligned to UCSC GRCh37/hg19 reference genome using Burrows-Wheeler Aligner (BWA). GATK Haplotype Caller was used to call variants from aligned reads. Variants were annotated using Annovar, prioritized according to American College of Medical Genetics and Genomics (ACMG) and the association with heart diseases was searched against various databases.
Results: Pathogenic or disease-causing mutations were identified in 36% individuals with SCD, likely pathogenic or potentially disease-causing mutation in 34%, disease- associated polymorphism or functional polymorphism in 6% as well as variants of unknown significance/likely benign/benign in 24%. Two novel variants in *MYH6* and *DPP6* genes were also identified. In addition, *KCNH2* R1047L which is associated with drug-induced torsades de pointes (TdP) was detected in two SCD individuals.
Conclusion: This landmark study on our local population revealed gene mutation profiles that causes SCD among Malaysians. Furthermore, cascade screening among the family members may be offered to identify high-risk individuals for preventive measures.

Keywords: Sudden cardiac death (SCD); coronary heart diseases (CHD); biomarker; early detection; genetic; cohort study

Development of Wearable Photoplethysmograph System for Healthcare Application

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Background: The industrial revolution has greatly influenced the use of technology for healthcare application. The internet of things and the use of wearable devices have improved the way people communicate and quality of living. Wearable electronics is one of the most rapidly growth industry in this decade. The use of sensors like optical sensor, ECG and EEG allows users to self-measurement of the physiological signals. Photoplethysmograph (PPG) is an optical method that measure blood volume changed associated with cardiac contraction. PPG signal can be obtained from earlobes, fingers and toes due to its low optical absorption and high degree of vasculature. However, most of the PPG devices are still bulky, wired connection and power consuming. Size and the cost of the system make it difficult for home based monitoring, elderly care and emergency setting. These wired PPG devices restrict the users' mobility and comfort level, especially during sleep or performing day to day activities. The high- resolution characteristic of the signal (24 bits) generates a huge quantity of data, difficult to deal with using conventional low-power wireless data transmission systems. As such there is a need to develop wearable PPG system that enables health monitoring that can overcome these limitations.
Methods: A wearable PPG system has been designed and developed which consist of BPatches (BPs) that are worn by the user and the Base Station (BS) that records the information sent by BPs. The Base Station (BS) is a Windows PC or laptop with a Bluetooth Low Energy (BLE) dongle attached. The BS runs the BPatch Control (BC) application to control the BPatches.
Results: In this study, PPG data of twelve healthy subjects (8 males and 4 females), age 23.8 $\pm$ 1.5 years have been recorded. Two BPatches with custom system each containing a photodetector and infrared light emitting diode (LED) were used to record the PPG signals from the carotid and toe for 90 seconds. Before data collection, each of the subjects' weight, height, the distance from the heart to carotid, distance from the heart to toe and BP from the right and left arms were recorded. The PPG signals were stored into SD card and retrieved using an acquisition software developed using MATLAB. All of the collected PPG signals were recorded at a sampling frequency of 500 Hz.
Conclusion: We have successfully developed a wearable PPG system using ultra

low-power wireless System on Chip (SoC). It can be used to measure heart rate, respiration rate, oxygen saturation and continuous blood pressure estimation based on pulse transit time.

Keywords: Photoplethysmograph, Wearable sensors, Low power

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