
ABSTRACTS OF

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ORAL PRESENTATION

PHYSIOLOGY

TOXICITY OF EXTRACT AND FRACTIONS OF PUSPA (*SCHIMA WALLICHII* KORTH.) BARK ON *ARTEMIA SALINA* LEACH

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Puspa (*Schima wallichii* Korth.) is a medicinal plant which has potential to be developed for anticancer treatment. Previous researches reported that puspa leaves have cytotoxic activity. In this present work, a toxicity test of extract and fractions of puspa bark was carried out by Brine Shrimp Lethality Test (BSLT). Extraction was done by maceration using 70% ethanol. The concentrated extract was dissolved in water and then fractionated by liquid-liquid extraction (LLE) using n-hexane and ethyl acetate respectively. The result of the toxicity test of ethanol extract and fractions of LLE indicated that all samples had a toxic effect on *Artemia salina* ($LC_{50} < 1000$ ppm). The highest toxic fraction was the ethyl acetate fraction ($LC_{50} = 24.70$ ppm), which has then further separated by classical column chromatography (CC). The group of fractions II from the CC process, showed the highest toxic activity ($LC_{50} = 11.40$ ppm). Preliminary identification of the active compound by phytochemical screening and TLC with several spray reagents, predicted that it was either terpenoid or polyphenol, however the identity of active compound is still unknown.

INVOLVEMENTS OF GABAERGIC SYSTEM IN ESSENTIAL OIL FROM *ZINGIBER ZERUMBET* INDUCED ANTINOCICEPTIVE ACTIVITY

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GABAergic system is one of the most important inhibitory systems in the CNS. Preliminary study on essential oil from *Zingiber zerumbet* (EOZZ) showed that it possesses central and peripheral inhibition of nociception. This study was conducted to verify GABAergic system participation in EOZZ induced antinociceptive activity. The involvements of GABAergic system were assessed by means of 0.6% acetic acid induced abdominal writhing test. Administration of GABA A and GABA B receptor antagonist (bicuculine and phaclofen, respectively) alone did not modify the effect caused by acetic acid injection. Intraperitoneal treatment of 200 mg/kg EOZZ produced 88% inhibition on

pain behavior induced by acetic acid. However, administration of 200 mg/kg EOZZ together with bicuculine showed reversal of pain behavior inhibition induced by 200 mg/kg EOZZ alone. Meanwhile, administration of 200 mg/kg EOZZ and phaclofen did not show any significant difference in the pain behavior induced by 200 mg/kg EOZZ treatment alone. In conclusion, EOZZ exerted its antinociceptive activity through the involvement of GABA A and not the GABA B receptor inhibition.

ANALGESIC ACTIVITY OF *EUPATORIUM ODORATUM* LEAVES EXTRACT

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Eupatorium odoratum (pokok kapal terbang) or *Choromolaena odorata* (synonym) is a wild weed plant which is easy to disperse and grow. Traditionally this plant is used to stop bleeding and heal the wound. Four different extracts (petroleum ether, chloroform, methanol and water) of *Eupatorium odoratum* were used for evaluation of potential analgesic activity using the tail flick and hot plate (paw) methods. The extracts were orally and intra peritoneally (IP) administered at a dose of 1 g/kg morphine where 10 mg/kg was adopted as the positive control and 4% of targacanth as negative control. Results showed that the water extract had analgesic effect for the hot plate but not the tail flick method. The water extract showed significant reduction ($p < 0.001$) at 30 min until 90 min. Further dose-response study of water extract showed dose-dependent activity at 0.5 g/kg and 1 g/kg. Subsequently the water extract was fractionated into three fractions (ethyl acetate, n-butanol and aqueous). The aqueous and ethyl acetate fractions showed significant ($p < 0.001$) analgesic activity. Further study is on going on phytochemical screening and identification of active chemical constituents in the active fraction. This study will continue with phytochemical screening to determine the compound inside this fraction.

DRUG**FRACTIONATION OF MELASTOMA MALABATHRICUM L. LEAF EXTRACT, OIL IN WATER CREAM FORMULATION OF THE EXTRACT FRACTIONS AND THEIR HEALING EFFECT ON BURN INJURY OF MALE RABBITS****NASUTION A., ARIS S. AND SURYANTO**Faculty of Pharmacy, University of Sumatera Utara,
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A study showed that melastoma extract at the concentration of 4.76% in a *vanishing cream* base healed burn injury of male rabbits in 23 days. Objectives of the study were to fractionate the *Melastoma malabathricum* extract components, formulate these fractionated extracts in a vanishing cream base and study their healing effects on burn injury of male rabbits. Standardised melastoma leaf was used for ethanol extract preparation by percolation. Ethanol extract was fractionated using solvents of different polarity by liquid-liquid extraction. As much as 4.76 g of each fractionated extract was formulated in 100 g of vanishing cream. The back side of the rabbits (n = 4 for each formula) was induced to obtain a second-degree burn injury. As much as 0.350 g of each cream formula was applied on the burned skin surface of the rabbits 3 times daily and were their effects observed for a period of 21 days. The melastoma extract contained 10.45% of water, 55.796% of water-soluble content 58.54% of ethanol-soluble content, 0.96% of ash content and 0.48% of acid-insoluble ash. The most effective cream was the one containing ethyl acetate-fractionated melastoma extract in which it healed the injury in 15 days. There was a significant difference among the 3 formulas at 15 day-treatments (Anova; $a \geq 0.05$; Duncan).

SURFACTANT MODIFIED SYNTHETIC ZEOLITE NaX AS SIMULTANEOUS ANTACID AND DRUG RELEASE SYSTEM FOR ACETYLSALICYLIC ACID**MALEK N. A. N. N.¹, YUSOF A. M.², RASHID N. A. A.¹
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Zeolite NaX modified with surfactants [hexadecyltrimethyl ammonium (HDTMA) and benzalkonium chloride (BKC)] was used to study their roles as antacid and support system for acetylsalicylic acid (ASA). Surfactant modified zeoliteNaX-ASA (SMZX-ASA)

composite was prepared via the addition of surfactants (2.0 mM) and ASA (0.5 mM) solutions with zeolite NaX. The performance of SMZX as a drug support system for ASA was investigated in simulated gastric fluid (SGF) through a time release study. Surfactant modified natural zeolite clinoptilolite-ASA (SMC-ASA) composite was used as a comparison. SMZX-ASA was able to release a high amount of ASA in SGF compared to SMC-ASA. Additionally, SMZX-ASA could act as an antacid since it can raise the pH of SGF to the desirable stomach pH operating condition. When compared to SMC-ASA, the pH of SGF after the release study was reduced thus indicating that clinoptilolite was not suitable as a drug support system. The characterisation of solid fraction after the release study was carried out using Fourier Transform-Infrared (FTIR) spectroscopy, Energy Dispersive X-Ray (EDX) analysis and Field Emission-Scanning Electron Microscopy (FESEM) and they revealed that the antacid properties of SMZX-ASA were basically due to the release of high amount of Na⁺ into the SGF. As a conclusion, synthetic zeolite NaX modified with surfactants (SMZX) could be used as simultaneous support system and antacid for ASA and furthermore its performance is better than natural zeolite.

FERROUS SULFATE BIOAVAILABILITY FORMULATED IN ALGINATE CAPSULE

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Ferrous sulfate in alginate capsule was designed to release iron slowly as the capsule retained in the stomach to prevent stomach irritation. This study aimed to test the bioavailability of ferrous sulfate formulated in alginate capsule compared to that in gelatin capsule on animal. The study was performed by cross over design with 2 weeks wash out period using 6 male rabbits. Each rabbit received 2 formulations, and blood samples were taken from the marginal vein until 540 min after administration of capsule under fasting condition. Iron level in serum was measured using atomic absorption spectrophotometer at a wavelength of 248.3 nm. Ferrous sulfate absorption in the alginate capsule had t_{max} of 115 min, the maximum iron concentration in rabbit serum (C_{max}) of 6.30 mcg/mL, and $AUC_{0-\infty}$ 1527.04 mcg.hour/mL, while ferrous sulfate in gelatin capsule had t_{max} of 60 min, the maximum iron concentration in rabbit serum (C_{max}) was 5.38 mcg/mL, and $AUC_{0-\infty}$ was 1283.52 mcg.hour/mL. These results indicated that the dosage of ferrous sulfate in alginate and gelatin capsules were bioequivalent and not different statistically for C_{max} and $AUC_{0-\infty}$ parameters, but they were not bioequivalent and different statistically for the t_{max} parameter.

PHASE DIAGRAMS BEHAVIOUR OF PALM KERNEL OIL ESTERS AND BLENDS OF NON IONIC SURFACTANTS

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Palm oil is the leading agricultural product of Malaysia. Palm kernel oil (PKO) is the oil obtained from the kernel of the nut. PKO is composed of saturated lauric acid, myristic fatty acids and unsaturated oleic acid. Its unique composition makes it versatile in various fields of application. Research bodies in Malaysia namely Malaysia Palm Oil Board, Palm Oil Research Institute of Malaysia and Universiti Putra Malaysia have modified PKO into palm kernel oil ester (PKOE) having improved properties for new applications. In this study the phase behaviours of PKOEs with low and high HLB blends of Tween® 80 and Span® 80 and water were studied. Various ratios of surfactant mixtures of HLB in the range 10.7–15.0 and surfactant:oil ratios of 1:9, 1:4, 3:7, 2:3, 1:1, 3:2, 7:3, 4:1 and 9:1 were prepared in separate universal bottle. Water was added drop wise to the mixture in an increment of 5%. Visual observation and microscopic examination of the mixture was recorded after each addition of water. The types of mixtures formed and the percentage of their components were used to construct phase diagrams. The results showed that the phase behaviour of mixtures is surfactant HLB dependent. Water in oil microemulsions, transitional liquid crystalline with high swelling capacity and other dispersion phases were formed. These dispersion phases might have a potential application in drug delivery and personal care products.

TASTE MASKING EVALUATION OF SWEETENING AGENTS ON DONEPEZIL

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Orally dissolving film is a thin film that is prepared using hydrophilic polymers, that rapidly dissolves in the oral cavity. The aim of this study was to perform a taste evaluation study to evaluate the effect of different sweetening agents on masking the bitter taste of donepezil hydrochloride. A thin film was developed using hydroxypropyl methylcellulose, corn starch, polyethylene glycol and crosspovidone as hydrophilic polymer base. Three kinds of sweetening agents namely sodium saccharin, aspartame and sucralose at different concentrations were used. A total of 16 healthy adult volunteers participated in this single-dose, randomised, fasting, four-period, eight-treatment, double blind study. Eight formulations with different amount of sweetening agent were tested. The in vivo disintegration time was taken and the volunteers were given a questionnaire

to fill. Five parameters were rated namely taste, after-taste, mouth-feel, ease of handling and acceptance. The score was analysed using Kruskal-Wallis test. It was found that formulation that contained 7 mg sucralose was superior to others in term of taste, mouth feel and acceptance. The in-vitro dissolution test was performed using USP paddle method; dissolution medium was distilled water at $37 \pm 0.5^\circ\text{C}$, at rotation speed of 50 rpm. The in vitro dissolution test showed that 80% of the active ingredient was released within 5 min and the mean disintegrating time was 44 s (n = 6). In vivo disintegration test yielded disintegrating time of 49 s (n = 16). In summary, an orally dissolving film was developed with fast disintegrating time and in vivo taste evaluation study suggested that bitter taste of donepezil could be successfully masked by 7 mg of sucralose.

THE COMPARISON OF EFFECT BETWEEN ASPIRIN GIVEN IN ALGINATE CAPSULE AND THAT GIVEN IN ENTERIC COATED TABLET

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Nowadays, aspirin is widely used as an antiplatelet and is still used as analgesic and antipyretic drugs. However, aspirin has a local side effect in the gastrointestinal tract causing injury and bleeding. The purpose of this study was to compare the effect of aspirin to the gastrointestinal tract between aspirin given in alginate capsule (gastric resistant capsule) and that given in enteric coated tablet. The effect of preparations was tested by chronic irritation test in rabbits. The test was conducted for 90 days. The rabbits were divided into three groups; each group consisted of six rabbits. The first group was the control group, without the administration of the preparation. The second group was given 80 mg aspirin in alginate capsules once a day. The third group was given 80 mg aspirin in the form of enteric coated tablets once a day. After 90 days of experiment all of the rabbits were killed and their stomachs, small intestines, and large intestines were macroscopically and microscopically (histopathologically) observed. It was found that aspirin in alginate capsules did not cause irritation along the gastrointestinal tract of all rabbits. However, two of the six rabbits given enteric coated aspirin tablets experienced duodenal irritations shown by the thinning of the epithelial cells and the dilation of blood vessels. The stomach and large intestine of all rabbits given enteric coated aspirin tablets were normal. It is concluded that aspirin given in alginate capsules is safer to the gastrointestinal tract of rabbits compared to aspirin given in enteric coated tablets form.

IN VITRO PERMEATION AND IRRITATION STUDIES OF NICOTINE PATCH BASED ON HPMC AND ETHYLCELLULOSE

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Nicotine patch is one of alternative therapies to stop smoking. The aim of this study is to formulate and evaluate nicotine patch. Nicotine patch (48.285 mg/patch) was formulated using hydroxypropyl methylcellulose and 5% ethylcellulose (4:1), isopropyl myristate (10%) as an enhancer, dibutylphtalate (1,25%) as a plasticizer, and polyisobutylene (2,5% in n-hexane) as an adhesive, and combination of methanol and chloroform (1:1) as solvents. In vitro permeability of nicotine was evaluated using the horizontal type of flow-through diffusion cells for 24 h and shed snake skin of *Phyton reticulate* as the membrane. The irritation study was done on the dorsal area of rabbits. The results of in vitro permeation of nicotine were $6.19\% \pm 3.03\%$ and $9.21\% \pm 1.30\%$ from the tested patch and commercial preparation (Nicotinell TTS 30), respectively. The nicotine patch did not cause skin irritation or gave any signs of oedema. In vitro permeation of nicotine patch showed similar profiles with commercial preparation but in lower amount. The mechanism of release of nicotine from the patch followed the Higuchi kinetic equation.

PHARMACY

GASTRIC TOLERANCE TOWARDS FERROUS SULPHATE GIVEN IN ALGINATE CAPSULES IN IRON DEFICIENCY ANEMIC PATIENTS

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Oral iron preparations of ferrous sulphate (FeSO_4) causes gastrointestinal side-effects such as epigastric discomfort, nausea, vomiting, abdominal pain, constipation, heartburn and diarrhoea. Alginate capsule is a gastric delivery system that releases FeSO_4 slowly during the time the capsule is retained in the stomach. The aim of this study was to evaluate the tolerance of the gaster towards FeSO_4 given in alginate capsules in iron deficiency anemic (IDA) patients with normal gaster (based on endoscopic observation). This study was done by randomised and double-blind design, using gelatin capsules as control. IDA patients were randomly distributed to receive FeSO_4 in alginate capsules or gelatin capsules (13 women in each group). FeSO_4 was given once daily an hour before breakfast at the dose of 300 mg (~60 mg Fe) for 4 weeks. The side-effects were confirmed by interviewing at the 7, 14, 21, and 28th days after the patients completed the daily card of

side-effects list including nausea, heartburn, full stomach, vomiting, constipation, diarrhoea and abdominal pain, and after endoscopic observation. Those data were analysed by χ^2 test. FeSO₄ in gelatin capsules caused a significantly higher frequency of nausea than that in the alginate capsules. Gastritis was found in the antrum of gaster of patients who received FeSO₄ in gelatin capsules, while there was no pathologic condition in the gastroduodenal of patients who received FeSO₄ in alginate capsules. In conclusion, 300 mg of FeSO₄ given in alginate capsules were tolerated by iron deficiency anemia patients with normal gaster.

THERAPEUTIC DRUG MONITORING OF GENTAMYCINE ON CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND COMMUNITY ACQUIRED PNEUMONIA

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A study on therapeutic drug monitoring of gentamycin toward chronic obstructive pulmonary disease and community acquired pneumonia had been performed at RSUP.H Adam Malik, Medan. The gentamycin bolus was given intravenously every 12 hours then the concentration of gentamycin in the blood was determined in the serum taken at 30 minutes after the first dose is administered in steady state. The second aliquot was taken 6 hours after injection of the first dose to find out the clinical manifestation, and the third was taken 5 minutes before injection of the second dose. Before and during gentamycin therapy, the patients (initials: MU, SU, MR, DI, RS, MR) were subjected to laboratory examinations covering complete blood, kidney faal (BUN and serum creatinin) and microba resistancy culture test. Based on the examination of gentamycin concentration in the blood by using chemistry autoanalyser (COBAS INTEGRA 400 Roche), it was found that MU had $C_{max} = 4.51$ mcg/mL, $C_{6hours} = 3.08$ mcg/mL, $C_{min} = 1.34$ mcg/mL; SU had $C_{max} = 4.13$ mcg/mL, $C_{6hours} = 1.42$ mcg/mL, $C_{min} = 0.52$ mcg/mL; MR had $C_{max} = 5.22$ mcg/mL, $C_{6hours} = 0.94$ mcg/mL, $C_{min} = 0.41$ mcg/mL; DI had $C_{max} = 8.41$ mcg/mL, $C_{6hours} = 6.83$ mcg/mL, $C_{min} = 2.41$ mcg/mL; RS had $C_{max} = 6.72$ mcg/mL, $C_{6hours} = 2.0$ mcg/mL, $C_{min} = 1.1$ mcg/mL; MR had $C_{max} = 4.32$ mcg/mL, $C_{6hours} = 1.35$ mcg/mL, $C_{min} = 0.9$ mcg/mL. The results of the study showed that gentamycin therapy of 80 mg every 12 hours without considering body weight and kidney function caused high variability towards the achievement of therapeutic concentration.

RETURNED MEDICATIONS COST: SCENARIO IN HOSPITAL PUTRAJAYA

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Health care management in Malaysia is being subsidised by the government. Medicine wastage in government hospitals has become a critical problem in the pharmaceutical care especially as a monetary implication. Of all the medications returned in the month of February 2010, it was found that majority of the drugs were reusable. The hospital was able to save USD 7852.50 from returned medications. According to the drug classes, antimicrobial drugs were accounted for the highest total saved from all wards (58.0%), while GIT drugs contributed to the highest total lost (29.0%). Of all the wards in this hospital, the ICU ward had the highest returned medications (18.4%) and also the highest level of wastage comparatively (USD 92.39). The majority component of this were GIT drugs (59.8%) followed by respiratory drugs (38.2%). Ward 2a and 2b (obstetrics and gynaecology wards) has contributed 29.0% of wastage cost from the antiinflammatory drug group. Ward 2c (paediatric ward) had the least returned medication (4.8%) and shared the same scenario with all the other wards, i.e. returned medication from the antimicrobial drug group was the most cost saving (31.3%). Drugs from the CVS group were the highest contributor of wasted drugs (72.0%) from ward 4b (general medicine and psychiatry ward). The wastage of medications has definite impacts environmentally and financially, hence diligence in patient medication supply and returned medication management is needed.

INFLUENCE OF PROMOTION MIX ON PURCHASE DECISION OF PATIENTS IN CHILDREN WARD OF MOTHER AND CHILD HOSPITAL, BANDUNG, INDONESIA YEAR 2007

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Basic tools that are used to accomplish company communication objectives is known as the promotion mix which includes advertising, sales promotion, public relation, and direct marketing. Purchase decision is a consumer's decision to buy a branded product.

Purchase decision influenced will lead customers to purchase frequently. Better promotion mixes will affect the frequency of purchase at Mother and Child Hospital. The research used the quantitative method and descriptive analysis. Sampling was done on about 100 individuals that have met the requirement of a child (child defined based on WHO criteria; aged between 1 month to 17 years). Patients ward criteria are hospitalised during December 2006–February 2007, have telecommunication tools, and the respondents are mother or mother-in-law of patients. Data is obtained by a questionnaire given directly or telephone dialed to the respondent. Data measurement is obtained by giving score to each question for each variable. Statistical analysis used are univariate analysis through frequency distribution, bivariate analysis through Pearson correlation and multivariate analysis through path analysis. In conclusion, it is found that promotion mix had a positive influence on purchase decision in the children's ward of Mother and Child Hospital. Contribution of each promotion mix directly and indirectly for advertising about is 0.27%, sales promotion about 4.68%, public relation about 20.44%, and direct marketing about 0.04%.

EVALUATION OF HYPERTENSION TREATMENT STRATEGY AMONG DIABETIC AND NONDIABETIC SUBJECTS IN MISURATA

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Hypertension is estimated to cause 4.5% of the current global disease burden. It has been stated that hypertension is at least twice as common in diabetic subjects when compared with the nondiabetic population. Clinical trials have convincingly demonstrated the importance of intensive treatment of hypertension among patients with diabetes. The study was mainly aimed to determine the proportions of patients who met or achieve the international goals (JNC7), to determine the pattern of the management and to assess the adherence of physicians to international guidelines. This study is a prospective descriptive study conducted at five medical centers in Misurata. Three hundred and eight cases were randomly collected and included in this study. Data obtained were computerised and analysed using SPSS version 17. The control of hypertension was unacceptable, as poorly reflected in the percentage where only 18.2% achieved the desired goal of antihypertensive therapy (less than 140/90 for nondiabetics and less than 130/80 for diabetics). Hundred and thirty nine patients (45.1%) belonged to stage 1 hypertension whereas 104 patients (33.8%) belonged to stage 2. Regarding drug utilisation, 54.5% of patients were on monotherapy and the most prescribed drug was Atenolol (30.5%). The most prescribed antihypertensive class was ACE inhibitors (45.7%) whereas the thiazide diuretics were underused. ACEIs and ARBs were not prescribed to 41.2% of the diabetic patients. There were 51 patients in the stage 2 receiving monotherapy. A great percentage of physicians (67.2%) depend on just one measurement. There is need for a more intense awareness program for doctors in our country regarding current blood pressure management guidelines and the need for adhering to them.

THE PATTERN OF SELF-MEDICATION AMONGST AIMST'S STUDENTS

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The study is to determine the pattern of self medication (S-M) among the students, the factors that contribute to S-M, and the students' opinions on such issue. A 300 self-developed, pre-validated questionnaire consisting of both open-ended and closed-ended questions were distributed randomly to AIMST students, and later 250 were able to be collected back from them. Of the 250 respondents, male: female ratio was 3:7, and ethnicity ratio of Chinese:Indian:Malay was 5:4:1. The prevalence of S-M was 58%. The commonest reasons for S-M were that the ailment was too mild to see the doctor (61.2%), followed by the reason of having previous experience of treating similar illness (50.8%). The common symptoms for S-M were flu (69.9%), headache (67.6%), and fever (53.6%). High proportion of students (92%), reported not encountering side effects with the use of S-M. The main source of medication for S-M is obtained from retail pharmacies (73%), and supply from family members (51%). 85% respondents read the labels on the medications, 74% followed strictly to the recommended dose, and 40% seek additional information regarding their medication. The level of satisfaction with S-M are as follows; 27.65% always satisfied, 59.25% sometimes satisfied, 10.00% rarely satisfied, and 2.00% never satisfied. Furthermore, a finer comparison between the medical and non-medical based students showed that prevalence of S-M is higher among the medical (64.8%), compared to non-medical based students (51.2%). When asked whether the respondents would continue S-M in the future, a stunning 88% of medical students, and 86% of non-medical based students agreed to continue such practice.

CAN SELF-REPORTING OF STRESS TASK ACT AS LABORATORY STRESSOR? INVESTIGATING THROUGH CVR-STRESS EXPERIMENT

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Cardiovascular reactivity (CVR) to stress is the magnitude of cardiovascular response that arises during time of challenge. Evidences of linkage between cardiovascular hyper-reactivity with future cardiovascular disease (CVD) had been established for a mean period of 10-15 years. CVR-stress experiments utilise different techniques to induce acute stress in the laboratory environment that should reflect the real stressful field situation. Trials are still performed to introduce novel stressors (challenges) that aim to be used universally as stable for all cases. Because the self-reporting of stress is a cognitive task that may induce affective and behavioral responses in humans, we introduced answering of *Stress in Academic Life Scale* (SALS) as an analogue stressor in the assessment of the CVR

magnitude during the experiment. The stress questionnaire was self-reported by a total of 124 pharmacy undergraduate students who participated in an experimental session which involved 2 continuous monitoring of cardiovascular blood pressure (BP) and heart rate (HR) biomarkers. Means of systolic BP, diastolic BP, and HR were 114 mm/Hg, 61.6 mm/Hg and 92.8 bpm respectively. CVR was counted using the maximum response analysis for both baseline and task monitoring. Comparison between the means of relaxation monitoring (readings during relaxation session) and monitoring during the task (readings during stressful session) has revealed no difference in magnitude of all the three reactivities for the whole sample or even for each demographic category. This rejection of the hypothesis suggests the inert psych-physiological role of such task as laboratory challenge.

THE RELATIVE LUNG BIOAVAILABILITY OF INHALED SALBUTAMOL FOLLOWING JET NEBULISERS AND ULTRASONIC-VIBRATING MESH NEBULISERS IN STABLE ADULT ASTHMATIC PATIENTS

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The urinary excretion of salbutamol over the first 30 min post inhalation is an index of lung deposition, termed the relative bioavailability of salbutamol to the lungs. This study was to determine the relative lung bioavailability in 16 stable adult asthma patients when they inhaled 1.5 mg/1.5 mL salbutamol via U22 MicroAir™ ultrasonic-vibrating mesh [high flow rate (HFR) and low flow rate (LFR)], and 5 mg/2.5 mL via Sidestream™ (SN) jet nebulised systems. The validated high performance liquid chromatography (HPLC) assay was used to determine the urinary concentrations of salbutamol following inhalation. When the urinary amounts were normalised for the percentage of the nominal dose and for the percentage of the dose emitted, there was no significant difference in the relative lung bioavailability of salbutamol between the LFR and HFR and also no significant difference in the relative lung bioavailability detected following inhalation by LFR and HFR compared to the SN. However, the ratio of the relative lung bioavailability of salbutamol with respect to normalised dose emitted, for the LFR and HFR with respect to SN was 2.0:1.0 and 1.8:1.0, respectively. In conclusion 1.5 mg/1.5 mL of salbutamol nebulised from U22 was equal to 5 mg/2.5 mL of salbutamol nebulised from the SN. This suggests that some guideline is required otherwise patients will be using the standard dose used in jet nebulisers (equivalent to 2.5 or 5 mg of salbutamol) when using the U22. This reduction highlights cost savings in dispensing the respiration solutions and diluents.

In addition, it is always an advantage to use a more portable method than the bulky nebulisers.

FONDAPARINUX AND LEPIRUDIN IN THE MANAGEMENT OF HEPARIN-INDUCED THROMBOCYTOPENIA: A RETROSPECTIVE ANALYSIS

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Patients with heparin-induced thrombocytopenia (HIT) require anticoagulation with non-heparin immediate acting anticoagulants. Lepirudin is an FDA approved agent for HIT management while fondaparinux is not. A retrospective study was conducted at King Khalid University Hospital of HIT cases diagnosed from January 2006 to December 2009. The diagnosis was based on a positive immunoassay test and clinical findings consistent with HIT presentation (50% decrease in platelet count from baseline, 5 or more days after starting heparin therapy). Twelve HIT cases were identified in which fondaparinux was used in five subjects while lepirudin was employed in the management of seven patients. The median age was 65 years in the fondaparinux group, and 55 years in the lepirudin group. Male patients represented 42% of the study population while 58% were females. The majority of identified cases were on heparin infusion (75%), while subcutaneous heparin and heparin flushes were used in 25% of them prior to HIT diagnosis. Frequencies of concomitant chronic diseases as well as other treatments including antiplatelets were similar between the two group ($p > 0.05$). The time for platelet recovery was similar between the two groups (median = 4 days for both arms; $p = 0.736$). However, fondaparinux therapy was associated with a greater area under platelet count compared to lepirudin (8179 vs. 5768 cell $\times 10^9 \times \text{day/L}$; $p = 0.0303$), and smaller nadir counts (89 vs. 44 cell $\times 10^9/L$; $p = 0.061$). This data suggests that fondaparinux is at least as effective as lepirudin in reversing platelet count following HIT.

**PERVASIVENESS OF ADVERSE DRUG REACTIONS ACCOUNTED
IN A TERTIARY CARE HOSPITAL OF KLANG VALLEY****ISMAIL N. E.¹, PONTO T.², CHIN K. L.², ABDULLAH N. A.³, ABDULLAH A.²,
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Hospital-based drug and poison information service is accountable in reporting and monitoring adverse drug reactions (ADRs) despite of the severity level to identify and quantify the risks associated with the consumption of drugs. This retrospective study was to determine the pattern of ADRs accounted in Hospital Tengku Ampuan Rahimah, a tertiary care hospital. Data in ADR national report forms (n = 214) between January 2007 and December 2009 were recorded and analysed descriptively. Overall in 3 consecutive years [2007: n = 52 (24.30%); 2008: 54 (25.23%); 2009: 108 (50.47%)], about 83.64%, 15.42% and 0.94% of pharmacists, physicians and nurses reported ADR cases, respectively. The occurrence of ADR was higher in female (67.76%) compared to male patients. The incidence of ADR was most frequently reported in the Malay ethnic (50.93%), and 33.64% were between 45–60 years old. Antibiotics (25.42%) remained the most implicated pharmacological class, followed by antihypertensive drugs (19.49%) and analgesics (16.10%). The dermatological system (43.70%) was the most commonly affected organ system, followed by the central nervous system (25.45%) and the gastrointestinal system (14.91%). About 71.50% of reactions subsided post discontinuation while 13.55% reactions reappeared after reintroducing the suspected drugs. The extent of ADR were reported as mild (34.58%), moderate (45.33%) and severe (20.09%). In terms of drug reaction relationship, approximately 29.44% were certain, 45.33% were probable, 16.36% were possible, 1.87% were unlikely and 7.01% were unclassifiable. About 71.03% patients recovered, 23.36% not yet recovered while the remaining (5.61%) is unknown post treatment. This ADR evaluations fostered likelihood for interventions primarily for the preventable ADRs to warrant safer drug use.

MEDICINAL**IN VITRO STUDY OF ANTIOXIDANTS ACTIVITY POTENTIAL OF
30% ETHANOLIC EXTRACTS DERIVED FROM TWO
PHYLLANTHUS SPECIES INDIGENOUS TO MALAYSIA**

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Phyllanthus niruri and *Phyllanthus urinaria* powdered extracts were prepared using 30% ethanol. The antioxidant activity of these extracts was evaluated in terms of total phenolic content (TPC) and 1, 1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging assays. Major contents of the two extracts were identified using high performance liquid chromatography (HPLC). Standardisation of the extracts to external references gallic acid (GA), corilagin and ellagic acid (EA) was performed using validated HPLC method. High TPC is shown by *P. niruri* and *P. urinaria* extracts and calculated as 361.25 ± 3.85 mg/g and 422.23 ± 6.08 mg/g dry weight (DW) GA equivalents (GAE), respectively. Stronger DPPH inhibition activity is shown by IC₅₀ values of 559.16 ± 4.36 µg/mL and 184.73 ± 0.33 µg/mL for *P. niruri* and *P. urinaria* respectively as compared to the IC₅₀ (437.67 ± 1.71 µg/mL) of standard ascorbic acid. GA, corilagin and EA are identified as major compounds of the extracts. Their content in *P. niruri* is 7.774, 4.74 and 12.623 mg/g, while in *P. urinaria* is 6.267, 6.88 and 18.000 mg/g of DW extract for GA, corilagin and EA, respectively. The results show the extracts as potential source of natural antioxidants that can be medically utilised as antioxidant and reactive oxygen species scavengers.

**THE DEVELOPMENT OF GCMS METHOD FOR THE DETECTION
OF AMINO ACIDS IN GELATIN SAMPLES**

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Gelatin is a high molecular weight polypeptide, obtained by the thermal denaturation of collagen, and is widely used in the food, pharmaceutical, cosmetic and other industries due to its unique properties. This work presents a development of the GCMS method for the detection of amino acids in gelatin samples. A simple derivatisation technique employing ethyl chloroformate as the derivatising reagent for amino acids was used. The

derivatised amino acids were separated on HP-5MS column at 80°C to 280°C and detected using GCMS employing both TIC and SIM mode. All of the common amino acid derivatives were detected except for arginine. This method has been successfully used to classify gelatin from different origin.

MODEL BUILDING FOR VIRTUAL SCREENING OF COMPOUND LIBRARIES FOR ANTICHOLINESTERASE ACTIVITY

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Recent studies have identified that acetylcholinesterase (AChE) accelerates the formation of amyloid fibrils and stable complexes with amyloid beta ($A\beta$) that produce the senile plaques characteristic of Alzheimer's disease (AD). Our aim was to identify a structure to be used for the virtual screening on commercially available compound libraries to predict their ability to interact with the $A\beta$ binding site thus preventing or delaying the degeneration of cholinergic neurons. The AChE crystal structures (PDB code: 1B41, 1EVE, 1JO7, 1N5M, 1N5R and 2HA2) were extracted from the protein data bank and the ligands removed. Nineteen standard acetylcholinesterase inhibitors were docked into the resulting structures using Auto Dock Software and the results analysed in order to find the most suitable model for virtual screening to identify peripheral anionic site (PAS) binding ligands. The docking results using a crystal structure of human AChE in complex with fasciculin II (PDB code: 1B41) have shown that most of the PAS ligands are bound near the aromatic residue Trp 286. This is in agreement with site directed mutagenesis studies. Therefore, the structure obtained from this crystal structure was found to be the most suitable for identifying PAS ligands.

DOSE-RESPONSE ATTENUATION OF AIRWAY HYPERRESPONSIVENESS AND INFLAMMATION IN ACUTE ASTHMATIC MICE FOLLOWING TREATMENT WITH A SYNTHETIC GERANYL ACETOPHENONE

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We have previously shown that 2,4,6-trihydroxy-3-geranylacetophenone (tHGA), a major compound of *Melicope ptelefolia*, disrupts the synthesis of cysteinyl leukotrienes via inhibition of 5-lipoxygenase (5-LO). In this study we have synthesised this compound and evaluated its therapeutic effect in an acute murine model of asthma. Following ovalbumin (OVA) sensitisation via combined intraperitoneal and inhalatory administration, Balb/c mice were treated with various intraperitoneal doses of tHGA (0.2, 2.0, 20.0 and

100.0 mg/kg bodyweight). Mice were then subjected to graded doses of methacholine challenge with an ultrasonic nebuliser and airway hyperresponsiveness was assessed by comparison of enhanced pause (Penh) responses in a whole-body plethysmography system (Buxco). All doses except 0.2 mg/kg caused a significant reduction of Penh. Analysis of bronchoalveolar lavage showed that all doses except 0.2 mg/kg caused significant reduction in airway eosinophilia, cysteinyl leukotriene, interleukin (IL)-4, IL-5 and IL-13 secretion. Similarly all doses except 0.2 mg/kg caused significant reduction in tissue inflammatory scores and goblet cell metaplasia. tHGA exhibits potent therapeutic effects in acute murine asthma and has great potential for further evaluation due to its non-steroidal nature and potent antiasthmatic effects.

GLUCOSAMINE ANALYSIS IN SHARK CARTILAGE USING HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

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Glucosamine is a natural polyhydroxylated amine sugar. This compound has efficacy for therapy of osteoarthritis, by maintaining the structure, stimulating the development and reducing the degradation of cartilage in the body. Shark cartilage contains polysaccharide, mainly chondroitin and glucosamine. According to researches, shark bone powder has antiinflammatory activity in male rats. Glucosamine are polar and have no sufficient chromophore groups that can absorb UV radiation, therefore an analytical method development through a derivatisation process is required in order for glucosamine to be analysed by high performance liquid chromatography (HPLC) UV-Vis detector with reverse phase system. Research conducted includes the shark bone mineral processing, preparation of standard solution, preparation of sample solution, determination of optimum conditions, validation of analytical methods, and analysis of glucosamine in the shark bone. Validation analysis determined the value of linearity (0.997), selectivity test (R_s 1.98), repeatability test with KV (%) (1.44%), LOD (0.789 ppm) and LOQ (2.63 ppm). The results of the concentration of glucosamine in the shark bone determined using the analytical validation method, analysed with HPLC 240 nm UV detector with a C18 column (Lichocart[®], 250 mm × 4 mm), mobile phase of aqua bidestilata:glacial acetic acid:methanol (89.96:0.04:10, pH 3.5) and flow rate of 1.2 mL/min, was 0.031%.

COMPUTATIONAL INVESTIGATION OF THE 5-HT_{2A} RECEPTOR BINDING INTERACTIONS OF STANDARD LIGANDS AND APORPHINES

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The 5-hydroxytryptamine 2A (5-HT_{2A}) receptor has been implicated in numerous psychiatric disorders, including schizophrenia and depression. Several aporphines have been found to have 5-HT_{2A} receptor binding activity. The aim of this study was to investigate the ligand-receptor interactions of standard 5-HT_{2A} ligands and aporphines. A 3D molecular model of the rat 5-HT_{2A} receptor was constructed by homology modeling against the known crystal structure of the human β_2 -adrenergic receptor (PDB ID: 2RH1). Docking studies were then conducted using Autodock4.0. The standard ligands and aporphines were found to interact with residues belonging to transmembrane domains 2, 3, 5, 6, 7 and extracellular loop 2 (ECL2). The proposed binding interactions involve three sets of residues: (1) Asp155 (3.32) forming a hydrogen bond with the protonated amine of the ligands, (2) an aromatic network consisting of Trp151 (3.28), Trp336 (6.48), Phe339 (6.51), Phe340 (6.52), and Tyr370 (7.43), and (3) Val156 (3.36), Thr160 (3.37), Leu229 (ECL2), Gly238 (5.42), Ser239 (5.43), Asn363 (7.36) as possible hydrogen bond acceptors or donors. These findings are in agreement with currently available experimental data and suggest that the model has the potential to predict ligand-receptor interactions at the molecular level.

THE EFFECT OF SEQUENCE ALIGNMENT LENGTH ON TEMPLATE SELECTION ON THE HOMOLGY MODELING OF HUMAN CYTOCHROME P450 2D6 (CYP2D6)

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Homology modelling is one of the important alternative techniques to X-ray crystallography and nuclear magnetic resonance (NMR) spectroscopy in structural determination of protein. CYP2D6 drug metabolising enzymes have excessively been studied prior to the successful determination of its 3D structure using X-ray crystallography. This study is one of the earlier works carried out before the crystal structure was solved. The aim of this study is to identify possible criteria to improve the quality of the 2D6 model. Four mammalian crystal structures (CYP2C8, CYP2B4, CYP2C9 and CYP2C5) were selected from the protein databank as templates for the CYP2D6 model. Multiple sequence alignment between the selected target and the template was

performed. Secondary structure prediction was generated based on the CYP2D6 sequence and the 3D models built based on each template. The quality of the models was evaluated using Ramachandran's plot. The models were superimposed with CYP2D6 crystal structure. The secondary structure prediction of CYP2D6 sequence was found significantly matched to the secondary structure prediction of the 3D structures of the CYP2D6 models. The stereochemical quality of CYP2D6 models adequately satisfied the Ramachandran plot requirements and were comparable to the stereochemical quality of the templates and CYP2D6 crystal structure. The superimpose of the models with CYP2D6 experimental crystal structure satisfied the MODOLLER requirement limit. The study shows that not only the sequence identity is the critical factor in template selection but also the alignment length of the sequence. It is also shows the important of primary and secondary structure prediction.

BIOLOGY

EXPRESSION OF TOTAL AND PHOSPHORYLATED FOCAL ADHESION KINASE IN HEP G2 HEPATOCELLULAR CARCINOMA CELLS

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Focal adhesion kinase (FAK), a 125kDa cytoplasmic non receptor tyrosine kinase protein plays a crucial role in mediating signal transduction pathways in cancer. Activation of FAK has been implicated in cellular processes including cell attachment, migration, invasion, proliferation and survival. Previously, it has been shown that hepatocellular carcinoma (HCC) progression is correlated to the expression of total FAK and phosphorylated FAK Tyr397. In the present study, Western blotting and immunofluorescence analyses were used to evaluate the expression and subcellular distribution of total FAK, phosphorylated FAK Tyr397, Tyr407, Tyr861, Ser732 and Ser910 in Hep G2 cells. Western blotting analysis demonstrated that FAK and phospho-FAK Tyr397 were highly expressed, phospho-FAK Ser910 was moderately expressed while phospho-FAK Tyr861 was expressed at minimally detectable level. Phospho-FAK Tyr407 and Ser732 were not expressed in this cell line. Immunofluorescence results detected the staining of FAK and phospho-FAK Tyr397 in the cytoplasm and cellular protrusions of the cells. Phospho-FAK Tyr861 appeared to be localised mainly in the cytoplasm. There was no nuclear staining detected for any of the phosphorylation sites studied. Total FAK and phospho-FAK Tyr397 were highly expressed in Hep G2 HCC cells. Localisation of phospho-FAK Tyr 397 to cellular protrusions may be crucial for acquiring invasive

phenotype. In addition, phospho-FAK Ser910 and Tyr861 were expressed in Hep G2 cells indicating that these phosphorylation sites may also have prominent roles in HCC. Further functional studies on these phosphorylation sites are needed to gain new insights on the role of FAK phosphorylation in HCC.

ETHNOBOTANICAL STUDY OF MEDICINAL PLANTS FROM MANGROVE FORESTS IN NORTH SUMATRA, INDONESIA

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The conservation of ethno medicinal plants of mangrove forests in North Sumatra is reported. Ethnobotanical data were obtained by using semi-structured interviews and field observations. Four field sites namely (1) Kuala Serapuh-Kuala Gebang, (2) Jaring Halus, (3) Pulau Sembilan and (4) Bandar Khalifah were selected. Traditional medicine practitioners in the four field sites were interviewed. Forty seven plant species of mangrove plants belonging to 23 families were identified in the 4 sites. The mangrove plants consist of 29 species of true mangroves and 18 species of mangrove associates. Based on our observation there are several local communities that commonly use nine mangrove plants, i.e. *Acanthus illicifolius*, *Avicennia alba*, *Bruguiera gymnorrhiza*, *Excoecaria agallocha*, *Rhizophora apiculata*, *Nypa fruticans*, *Sonneratia alba* and *Xylocarpus granatum* for curing various diseases. Indigenous knowledge of mangrove plants as medicinal material was relatively different between field sites where Jaring Halus community was the highest user of mangrove plants (seven species), followed by Serapuh community (three species) and Banda Khalifah community (one species). None of the mangrove plant is used as a medicinal plant by the Pulau Sembilan community. The decreasing population of mangrove plant community is due to the wide destruction of mangrove sites. Apparently with this massive destruction, several species of medicinal plants are destroyed. Therefore this result can be used as a basis for developing management plans for conservation and sustainable use of medicinal plants in the area.

POSTER PRESENTATIONS

MEDICINAL

DEVELOPMENT AND VALIDATION OF RP- HPLC SIMULTANEOUS DETERMINATION OF HYDROCHLORTHIAZIDE, RAMIPRIL AND TELMISARTAN IN TABLET DOSAGE FORM

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A simple, sensitive and specific liquid chromatographic method with UV detection (228 nm) was developed for the simultaneous estimation of hydrochlorothiazide, ramipril and telmisartan in tablet dosage form with bisoprolol as the internal standard. Separation was achieved with a phenomenex luna 5 μ C18(2) 100R, 250 \times 4.60 mm 5 μ size column, ambient temperature with a low pressure gradient mode with mobile phase containing acetonitril, 0.5% of potassium dihydrogen phosphate buffer (pH 3.8) adjusted with orthophosphoric acid (60:40). The flow rate was 1 mL min⁻¹ and the eluent was monitored at 220 nm. The selected chromatographic conditions were found to effectively separate hydrochlorothiazide, ramipril and telmisartan with retention time of 3.1, 5.0 and 13.8 min respectively. The linearity range of hydrochlorothiazide, ramipril and telmisartan found in the range of 2-10 μ g mL⁻¹, 5-25 μ g mL⁻¹ and 10-50 μ g mL⁻¹, respectively. The proposed method was found to be accurate, precise, reproducible and specific and it can also be used for routine quality control analysis of these drugs in combination tablets.

IDENTIFICATION AND CHARACTERISATION OF SIMPLEX CORAL *PAVONA CACTUS* FORSKAL (PHYLUM COELENTERATA) OBTAINED FROM SIBOLGA SEA, INDONESIA

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Pavona cactus (cactus coral) with flower-like morphology is included into phylum Coelenterata and class Anthozoa. In the field of pharmacy, the coral is used for orthopedic related treatment and as supplements for calcium-deficient patients. Studies on bioactive contents of corals from the Phylum Coelenterata have found that terpenoids are the dominant compounds. The objectives of this study were to identify and characterise the coral simplex that is part of the simplex standardisation, to identify and quantify the content of calcium (Ca) and lead (Pb), and to identify the presence of steroid/triterpenoid in coral animals. In conjunction with this study, the coral has been identified and named as *P. cactus* Forskal by the Indonesian Institute of Sciences, Research Centre for Oceanology. The sample was cleaned, dried, sorted, weighed, and refined. In this study,

water content was analysed by means of azeotropic distillation, whereas water soluble extract, ethanol soluble extract, total ash content, and acid insoluble ash were analysed by using the gravimetry method. Qualitative and quantitative analyses for metal substances using atomic absorption spectroscopy (AAS) have been done. Based on the analysis of simplex characteristics, water content of 0.99%, water soluble extract of 0.79%, ethanol soluble extract of 1.43%, total ash content of 54.67%, and acid insoluble ash of 10.04% was determined. The result of chemical screening showed the presence of steroids/triterpenoid. Qualitative analysis of metals of the marine coral showed the presence of Ca and Pb. AAS method indicated that the Ca concentration was 729.27 µg/g and the Pb concentration was 13.07 µg/g at wavelengths of 422.7 nm and 283.3 nm, respectively.

VALIDATION METHOD ON AMINO ACID DETERMINATION USING 6-AMINOQUINOLYL-N-HYDROXYSUCCINIMIDYL CARBAMATE (AQC) FOR HARUAN (*CHANNA STRIATUS*) AQUEOUS EXTRACT

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A quantitative method for amino acid analysis has been validated to analyse haruan aqueous extract. The method used 6-aminoquinolyl-n-hydroxysuccinimidyl carbamate (AQC) as the derivatisation reagent and also the auto-sampler, Waters reverse phase high performance liquid chromatography system with fluorescence detector. The parameters of validation i.e. specificity, system suitability, linearity, detection and quantification limit, accuracy, inter and intra assay precisions were studied for the amino acid standard and haruan aqueous extract. The peak area ratio varied linearly with concentration ranging from 50 to 300 pmole/µL corresponding to the concentration found in the haruan aqueous extract. The linearity varied for each amino acid from 0.9981 to 0.9999. Detection limits were from 0.01 to 0.09 ng/µL and quantification limits varied from 0.06 to 0.25 ng/µL. Inter and intraday assay precisions (CV) varied from 0.86% to 9.20%. Average analytical accuracy ranged between 97.0% to 100.29%. The method can be utilised as a quantification method for the determination of amino acid in biological products like haruan aqueous extract.

MICROPLATE-BASED CHARACTERISATION OF THE M₁ MUSCARINIC RECEPTOR BINDING ACTIVITY OF SELECTED FLAVONOID COMPOUNDS

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Alzheimer's disease (AD) is associated with poor or loss of cholinergic functions. It may be caused by insufficient acetylcholine production or inefficient binding to the M₁ muscarinic postsynaptic receptors. Thus, one possible approach to the treatment of AD is the use of M₁ selective agonists. An alternative approach is to use allosteric modulators which are able to increase the affinity of acetylcholine at the orthosteric site. The aim of this study was to investigate the M₁ muscarinic receptor binding activity of a library of flavonoid compounds. Microplate-based radioligand binding assays were utilised for the characterisation of the orthosteric and allosteric binding profiles of the test compounds using cloned human M₁ receptor membranes and [³H] N-methylscopolamine. Several compounds were found to possess orthosteric binding activity ($K_i \approx 10^{-5}$ M), while others exhibited positive or negative allosteric cooperativity with acetylcholine. These results confirmed that flavonoids have potential as M₁ muscarinic receptor active compounds.

OPTIMISATION OF METHANOL-WATER AS MOBILE PHASE FOR ANALYSIS OF PARACETAMOL AND CAFFEIN MIXTURE IN TABLET BY HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC)

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The purpose of these experiments is to optimise the high performance liquid chromatography (HPLC) condition using Shim-pack VP-ODS (4.6 mm × 25 cm) column and UV-Vis detector at 254 nm wavelength for the determination of paracetamol and caffeine mixture in tablet. Optimisation was done by modification to the Paszti and Forgacs method. To get the optimum condition of analysis, the mobile phase and flow rate have been varied. Optimisation result showed the best analysis condition was the mobile phase consisting of methanol-water (35:65) with 1 mL/min flow rate and retention time 4.18 min for paracetamol and 6.18 min for caffeine. The determination of calibration curve linearity showed the correlation coefficient, $r = 0.9999$ with the regression $Y = 48988.0735 X + 4696428.75$ for paracetamol and $r = 0.9999$ with the regression $Y = 29557.245 X + 10364.85$ for caffeine. The result for paracetamol and caffeine mixture in tablets was all samples were over than the required level that is that it contains paracetamol and caffeine not less than 90.0% and not more than 110.0%. In this case paracetamol in all samples were over 110.0%, whilst caffeine was in agreement with requirement. In conclusion, this method fulfilled clauses of validation test method with the percentage recovery at 100.35% for paracetamol and 98.69% for caffeine, standard deviation (SD) 0.1591 for paracetamol and

0.0775 for caffeine, relative standard deviation (RSD) 0.1585% for Paracetamol and 0.0786% for caffeine, limit of detection (LOD) and limit of quantification (LOQ) of paracetamol = 81.20 mcg/mL and 270.66 mcg/mL; LOD and LOQ of caffeine 0.91 mcg/mL and 3.06 mcg/mL, respectively.

PHYTOCHEMICAL STUDY OF *BAUHINIA VARIEGATA*, A RARE TREE IN MALAYSIA

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Bauhinia variegata is a species of flowering tree from the family Fabaceae, native to southeastern Asia. In the Indian sub-continent it is known as *kachmar*. *Kachmar* buds is a favourite vegetable dish when cooked in meat, in the Punjab area of the Indian sub-continent. It blooms in late winter till the end of April. The flowers of the tree are attractive to bees and butterflies. Pharmacologically the buds are said to be useful in treatment of numerous disorders. The tree is listed as an endangered species. Chemical groups identified so far from the tree are steroids, tannins, carbohydrates, amides, reducing sugars, ascorbic acid, proteins, anthraquinones, flavonoids, alkaloids, glycosides, calcium and phosphorous. For this study, this tree was found accidentally, located near the Subaidah Restaurant in Universiti Sains Malaysia (USM) Pulau Pinang by one of the author. Phytochemical analysis for some of the chemical groups from the aqueous and ethanolic extracts by maceration and soxhlet extraction was carried out on the buds, petals and dried crushed petals (under glass shade sunlight). The extracts were diluted with the respective solvents before analysis. The macerated and percolated extracts were of different colours and variable thickness. Aqueous and alcoholic extracts by maceration were found to be greasy and it is assumed that it may contain some lipo-protein or gummy type of chemicals. All the extracts which underwent qualitative tests, showed distinctive presence of alkaloids, reducing sugars, terpenoids, glycosides, tannins, flavonoids and carbohydrates. Saponins were not identified in any of the extracts and anthraquinones were also not detected in the aqueous extracts. A long term research project is needed for quantitative evaluation of the phytochemical constituents and their usefulness in medicine.

**SYNTHETIC CHALCONES INHIBIT PROINFLAMMATORY
MEDIATOR SECRETION IN LPS-INDUCED MACROPHAGE AND
ENDOTHELIAL CELLS**

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Chalcones are a subgroup of flavonoid compounds and have been shown to be potent inhibitors of proinflammatory mediator synthesis. Two synthetic chalcones, 3-(2, 5-dimethoxyphenyl)-1-(5-methylfuran-2-yl)prop-2-en-1-one (L31) and 3-(2,3-dimethoxyphenyl)-1-(5-methylfuran-2-yl)prop-2-en-1-one (L77) were evaluated for inhibitory effects upon major proinflammatory mediator secretion. MTT assays showed that both compounds were cytotoxic to cell lines at 25 μ M and above, and further assays were conducted at various non-toxic concentrations. Lipopolysaccharide (LPS) induction of the RAW 264.7 monocytic macrophage caused significant increases of nitric oxide (NO) secretion as measured by the Griess assay, and this was inhibited by both L31 and L77 with IC₅₀ values of 6.62 and 8.84 μ M, respectively. Following TNF- α induction of the HUVEC cell line, secretion of proinflammatory cytokines monocyte chemoattractant protein (MCP)-1, interleukin (IL)-6 and IL-8 were significantly increased and both L31 and L77 caused a dose-dependent inhibition of both MCP-1 and IL-6 with IC₅₀ values of 11.53 and 12.72 μ M, respectively. However both compounds failed to inhibit the secretion of IL-8. These synthetic chalcone analogues demonstrate partial selectivity in mediator inhibition and are potent antiinflammatory drug leads that warrant further investigation.

**BHMC ATTENUATES LPS-INDUCED VASCULAR
HYPERPERMEABILITY, ADHESION MOLECULE EXPRESSION,
AND TRANSENDOTHELIAL MIGRATION VIA SELECTIVE
DISRUPTION OF P38 MAP
KINASE ACTIVITY**

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Curcumin is a potent antiinflammatory drug lead but has poor bioavailability in animals and man. We have synthesised 2, 6-bis-(4-hydroxyl-3-methoxybenzylidene) cyclohexanone (BHMC), a synthetic diarylpentanoid curcuminoid analog to enhance bioavailability. In this study, the effect of BHMC upon vascular hyperpermeability, expression of intercellular adhesion molecule (ICAM)-1 and monocyte-endothelial adhesion and transendothelial migration, was compared to that of curcumin. Treatment

of LPS-induced human umbilical vein endothelial cells (HUVECs) with BHMC caused a 3-fold decrease in the expression of ICAM-1 and this attenuation was 2-fold higher than that of curcumin. BHMC also attenuated the adhesion and transendothelial migration of U937 monocytes through LPS-induced HUVEC layers by $88.34 \pm 12.83\%$ and $68.03 \pm 10.19\%$ respectively. This effect was significantly more potent compared to that of curcumin. Several proinflammatory signaling pathways were evaluated to determine the molecular target of BHMC and we show that BHMC is much more selective in comparison to curcumin. Whereas curcumin disrupts the NF- κ B, JNK, ERK1/2 and p38 pathways, BHMC only specifically acted upon p38 MAP kinase activity as determined through the inhibition of ATF-2 phosphorylation. We further employed silico molecular docking methodology to show that BHMC fits well in the ATP pocket of p38 MAP kinase. Structural modification of curcumin into BHMC incurred a more selective mode of action with enhanced potency upon vascular inflammatory processes.

DRUG

FORMULATION AND IN VITRO EVALUATION OF MUCOADHESIVE POLYMER BASED GASTRORETENTIVE TABLETS OF ATENOLOL

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The objective of the present work was to formulate controlled release floating tablets of Atenolol using polyethylene oxide and HPMC K4M as matrix polymers. The floating tablets containing Atenolol (dose of 120 mg) were prepared by direct compression technique. A total of 12 formulations were prepared using different ratios of drug and polymers. The tablets were evaluated for physical properties, in vitro dissolution (USP Type I) as per the standard procedures specified in the USP. The prepared tablets were evaluated for weight variation, hardness, thickness, swelling index, in vitro floating capabilities, floating lag time, drug content uniformity, compatibility and in vitro drug release studies. From the study it was found that the floating lag time of the tablet ranges from 8 to 90 seconds and all the formulations floated for more than 8 hours. The results showed that the optimised formulation had good floating capability, shorter floating lag time, and sustained drug release for 8 hours. Data analysis showed that the release profile obeyed Korsmeyer-Peppas equation showing non-Fickian release.

IN VITRO ANTITUMORAL ACTIVITY OF TAMOXIFEN-LOADED SOLID LIPID NANOPARTICLE

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Recently, solid lipid nanoparticles (SLNs) have been recommended as drug delivery system for the formulation of poor water soluble drugs like tamoxifen (TAM). In this study, TAM at concentration of 20% with respect to SLN was loaded into the SLN by high pressure homogenisation technique and then the chemotherapeutic effect of TAM-loaded SLN on breast cancer cell lines, MCF-7 and MDA-MB231 was determined in vitro. The responses of the cell lines were studied by MTT assay, cellular and nuclear morphology, apoptosis and cell cycle distribution. The TAM-loaded SLN showed similar antitumoral activity against the cells as free TAM. The apoptotic cell death was recognised under phase contrast and fluorescence inverted microscope after staining. Morphological features of the TAM- and TAM-loaded SLN- treated cells revealed detachment of both the breast cancer cells and loss of colony formation ability. The results of cell cycle distribution showed dose- and time-dependent apoptosis that resulted from TAM-loaded SLN and TAM treatment of the cells. The obtained apoptosis was demonstrated to be independent cell cycle arrest. Fluorescence microscopy results revealed that TAM and TAM-loaded SLN induced the cell death by apoptosis. The apoptosis was evident by the typical apoptotic changes showing clear condensation of cell nuclei, nuclear fragmentation and apoptotic bodies. Therefore the TAM-loaded SLN can be considered as an alternative formulation for the antiestrogen drug, tamoxifen, in the treatment of breast cancer.

DISSOLUTION TEST OF FERROUS SULPHATE FORMULATED IN ALGINATE AND GELATIN CAPSULES

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The research was done to provide a dosage formulation of ferrous sulphate with ascorbic acid and lactose that prevents the oxidation of ferrous sulphate in order to increase the absorption of iron. Ferrous sulphate formulations utilised alginate capsules to prevent stomach irritation. Dissolution was also done to compare the release of ferrous sulphate in alginate and gelatin capsules in medium of different pH for 240 minutes; pH 1.2 for 120 minutes, then pH 4.5 for 30 and pH 6.8 for 90 minutes. Addition of 50 mg of ascorbic acid and lactose were found to prevent the oxidation of ferrous sulphate and increased water

absorption. Release of ferrous sulphate in alginate capsule containing ferrous sulphate alone and with preparations containing ascorbic acid and lactose was not different until the 45th minute, but after 45 minutes the preparation with the addition of ascorbic acid and lactose was found to increase the release of ferrous sulphate. Release of ferrous sulphate in alginate capsule reached maximum after 60 minutes, whilst in gelatin capsule it was after 10 minutes. Ferrous sulphate release rate formulated in alginate capsule was slower than ferrous sulphate formulated in gelatin capsules.

FORMULATION AND EVALUATION OF IN SITU GEL BASED DRUG DELIVERY SYSTEM OF PILOCARPINE

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Novel in situ gel based drug delivery system was developed for pilocarpine hydrochloride using chitosan and sodium glycerophosphate. Formulations were in solution form at lower temperatures and transformed into gels when instilled into the cul-de-sac of the eye. The in situ prepared gels were evaluated for various parameters such as viscosity, content uniformity, sterility, in vitro release and in vivo studies. Results indicated that viscosity of the gels increased with increase in the polymer concentration and temperature, and drug concentration had little or no effect on the viscosity of formulations. All the formulations were ascertained to be sterile as there was no bacterial growth even after 14 days. The in vitro release studies showed that pilocarpine hydrochloride was released from in situ gels in a sustained manner. The drug release from the formulations was by Fickian diffusion and followed the first order kinetics. Higuchi plot confirmed that the drug release was by diffusion controlled process. In vivo studies were carried out on rabbits. The optimum formulation was non-irritant with good gelling property and faster recovery. Hence, it may be concluded that in situ gel formulations of pilocarpine hydrochloride is a novel approach and improves patient compliance.

DEVELOPMENT AND VALIDATION OF A RAPID RP-HPLC METHOD FOR SIMULTANEOUS DETERMINATION OF CURCUMINOIDS AND QUERCETIN

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A simple, rapid reversed-phase high performance liquid chromatographic (RP-HPLC) method was developed and validated for simultaneous quantification of curcuminoids and quercetin in pharmaceutical formulations. The analysis was performed using a C₁₈ column (250 × 4.6 mm, 5 μm) by isocratic elution at 370 nm. Good separation of quercetin, curcumin, DMC, BDMC was achieved using acetonitrile: 2% acetic acid (42:58 v/v, pH

3.0) at a flow rate of 1.3 mL/min. The standard calibration curve was linear over the concentration range studied (quercetin: 0.625–180 µg/mL; curcumin, DMC, BDMC: 1.25–200 µg/mL). The limits of detection and quantification (LLOQ) were 0.039 and 0.625 µg/mL for quercetin, 0.078 and 1.25 µg/mL for curcumin, 0.313 and 1.250 µg/mL for DMC, 0.625 and 1.250 µg/mL for BDMC. LLOQ, and three quality control samples (3.5, 100, 180 µg/mL for curcumin, DMC and BDMC; and 2.5, 80, 140 µg/mL for quercetin) were used for intra- and inter-day precision and accuracy studies and system suitability validation. The mean recoveries (n = 6) for intra-day analysis were 98.83%–101.43% (RSD ≤ 0.81%) for quercetin, 99.20%–100.65% (RSD ≤ 1.35%) for curcumin, 99.01%–101.92% (RSD ≤ 1.51%) for DMC and 97.75%–99.36% (RSD ≤ 1.94%) for BDMC, and inter-day analysis were, respectively, 98.50%–101.75% (RSD ≤ 1.91%), 99.54%–102.58% (RSD ≤ 1.35%), 101.2%–102.64% (RSD ≤ 1.55%) and 99.79%–101.77% (RSD ≤ 1.47%). The system suitability data, namely, number of theoretical plates, resolution, capacity factor and tailing factor, were within the required limits. The developed HPLC method is suitable for routine quantification of curcuminoids and quercetin in industrial quality control laboratories.

FORMULATION OF CHITOSAN THIXOGEL WITH CORN STARCH BASE

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Thixogel technology is an alternative method of gel formulation that contains hydrophobic active compounds, such as chitosan. Thixogel technology employs a low concentration of nonirritating surfactants in order to achieve oil dispersion in an aqueous starch matrix. This method is far superior to the prior art, the jet cooking process employed in the Fantesk process. In addition, in the thixogel technology, silicone oils have been either substituted for, or combined with, mineral oil and petrolatum in order to achieve finer dispersion of oil droplets and reduce the stickiness of the humectant-plasticised starch. The basic ingredients of all thixogel formulations are water, starch, oil, and an emulsifying agent. The starch component may be comprised of different natural and modified starches. The purpose of this study was to evaluate corn starch as a gel forming base in chitosan thixogel formulation. The organoleptic, physical stability, microbiology, and irritation tests were carried out to characterise the chitosan thixogel. Thixogel formulations were prepared with various corn starch concentration (2.5%; 3.5% and 4.5%). The result of physical and chemical stability testing showed that in 56 days, there were no changes in the organoleptic characteristic. The viscosity and pH values increased. The microbiological testing showed that there was no bacteria growth found in all formulas. The formula containing 3.5% of corn starch was the best formula in all aspects. Patch test showed that all formulas of chitosan thixogel can be safely used for human skin.

FORMULATION AND EVALUATION OF COMPACT POWDER WITH ETHYL ASCORBYL ETHER IN ALLYL METHACRYLATE CROSSPOLYMER (AMP) AS DRUG DELIVERY

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A research on the formulation of solid powder dosage in various concentrations of ethyl ascorbyl ether with a mixture of ethyl allyl methacrylate crosspolymer (0.5% and 1.0%) and compact powder with ethyl ascorbyl ether (0.5% and 1.0%) was carried out. Research goal is to formulate a solid powder cosmetic composition including the composition between the phases of powder and binder phases, which can provide favourable characteristics such as the regulation of sebum and improving the fineness of texture without causing a heavy feeling to the skin surface. Entrapment and characterisation of ethyl ascorbyl ether with ethyl allyl methacrylate crosspolymer had three formulas to be tested with comparisons made between ethyl ascorbyl ether solution of ethyl methacrylate with allyl crosspolymer (6:1, 8:1 and 10: 1). After getting the best formula, then it was dried over a waterbath for 15 minutes at a temperature of 50°C. After dried powder was obtained, the size and shape of particles was studied using scanning electron microscope (SEM). From the observations, it is known that the consistency, colour, odour, and homogeneity of the preparations were stable during the 28 days of storage. SEM test results, showed that the ethyl ascorbyl ether formula in the ethyl allyl methacrylate crosspolymer (1%) had particle size of 5–10 µm. Based on smoothness, spread quality, and adhesiveness in 20 females, ethyl ascorbyl ether in allyl methacrylate crosspolymer (1%) had the highest score. Based on physical evaluation, it was found that the compact powder preparation had good stability. The safety investigation of compact powder with ethyl ascorbyl ether in allyl methacrylate crosspolymer (1%) gives nonirritation on consumer's skin.

PHYSIOLOGY**A NOVEL DATA ACQUISITION SYSTEM IN STEPPING FORCE AN ANALGESIMETER**

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Behavioural assessment is an essential method for analysing and measuring the level of pain. Rodent models which are widely used in the behavioural test often undergo external forces and stressful manipulations that cause variability of the parameters measured during the experiment. In this report, a stepping-force analgesimeter was developed to investigate the variations in the stepping force of rats in response to pain induction. The proposed apparatus fabricated a new feature by equipping an infrared charge-coupled device (CCD) camera to capture the locomotion and a data acquisition system to capture the locomotion and synchronise the stepping force of the rat. Inter-day and intra-day precisions and accuracy of each channel was studied. The average mean values of precision and accuracy of the device were less than $\pm 1\%$ within 6 days of measurement. The validation studies for each channel also showed convincing results whereby intra-day and inter day precisions were less than 1% and accuracies were 99.36%–100.36%. Then, an in vivo test was carried out using 16 rats (8 females and 8 males). There were $50.27 \pm 3.90\%$ (male rats) and $62.20 \pm 6.12\%$ (female rats) of total movement which generated more than 2 peaks and did not fulfil the assumption mentioned by previous studies. As a result, we also found that $48.80 \pm 4.01\%$ (male rats) and $66.76 \pm 5.35\%$ (female rats) of total movement is needed to use the video display frame to identify the front paw or hind paw. Accordingly, the assumption of the present study is not realistically applicable for stepping force measurement. Hence, the use of video display frame is essential for observation to identify the front and hind paws through the peak signal.

ANTIINFLAMMATORY PROPERTIES OF *MELICOPE PTELEFOLIA* ETHANOLIC EXTRACT ON ACUTE AND CHRONIC INFLAMMATION INDUCED RATS

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Antiinflammatory properties of *Melicope ptelefolia* ethanolic extract were evaluated by carrageenan induced paw oedema and cotton pellet granuloma tests in albino Sprague Dawley rats. In the acute study, 1% carrageenan was injected subcutaneously into the subplantar region of the right hind paw. The paw oedema was measured at 0, 30, 90, 150, 210, 270, 330 and 330 min time intervals. Different doses of MPEE, administered orally 30 min before experiment at doses of 10, 30, 100 and 300mg/kg, produced significant and dose dependant inhibition. Meanwhile for chronic inflammation, cotton pellet-induced granuloma test was conducted for seven consecutive days. Sterile cotton pellet (20 mg/pellet) was implanted subcutaneously at the right and left of the dorsal region of the rats. Different concentration of MPEE was orally administered for seven days. On the eighth day, rats were sacrificed and cotton pellets with granuloma tissue were dissected out and weighed (wet and dry). Blood serum was collected for biochemical analysis. The highest dose of MPEE (300 mg/kg) has significantly inhibited formation of granuloma tissue. However, no significance was found at all doses of MPEE on level of total protein, ALP and ALT in blood serum. Aspirin was used as a positive control drug and showed significant inhibition towards both tests. These results suggest that MPEE acts very well on acute inflammation compared to chronic inflammation.

ANTIINFLAMMATORY EFFECT OF SIDAGURI (*SIDA* *RHOMBIFOLIA* L.) EXTRACT ADMINISTERED ORALLY AND TOPICALLY ON CARRAGEENAN-INDUCED MICE

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Synthetic antiinflammatory drugs may cause serious side effects, and therefore traditional medicine derived from plants could serve as an alternative treatment that has lesser side effect. One of the plants that have long been used by people for such purpose is sidaguri (*Sida rhombifolia* L.). The aim of this research was to test the antiinflammatory activity of

sidaguri administered orally and topically, in mice which were induced inflammation by λ -carrageenan 1% (w/v). Indomethacin was used as the positive control drug. Sidaguri plant extracts were made by percolation with ethanol (EES), *n*-hexane (En-HS), and ethyl acetate (EEAcS). The results showed that the EES has antiinflammatory activity similar to that of 10 mg/kg BW indomethacin, while En-HS and EEAcS did not show antiinflammatory activity. EES preparations gave good results as an antiinflammatory at doses of 400 mg/kg BW. Ethanol extract of gel (GEES) showed similar results with that of Na-diclofenac gel 1%. GEES tested gave good antiinflammatory results at concentration of 1%.

ANTIINFLAMMATORY EFFECT OF MONDOKAKI LEAVES [*TABERNAEMONTANA DIVARICATA* (L.) R.Br.] ETHANOL EXTRACT APPLIED ORALLY AND TOPICALLY

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Non-steroidal antiinflammatory drugs may cause many adverse effects. Therefore, the therapeutic management of inflammation recently shows the trend is shifting towards using plant materials. One of the plants traditionally used to ease inflammation is the Mondokaki plant (*Tabernaemontana divaricata* R.Br). The aim of this study was to evaluate the antiinflammatory activity of Mondokaki leaves ethanol extract applied both orally and topically. This study was conducted in a complete randomised experimental design. Mice were injected by 1% (w/v) λ -carrageenan to induce inflammation; indomethacin was used as positive control in oral administration whereas Na-diclofenac gel was used in topical administration. The Mondokaki leaves were extracted by percolation method using ethanol (MEE = Mondokaki ethanol extract), *n*-hexane (MNE = Mondokaki *n*-hexane extract), and ethyl acetate (MEAcE = Mondokaki ethyl acetate extract). The results showed that both MEE and MEAcE had same antiinflammatory activity with indomethacin dosage of 10 mg/kgBW ($n = 6$; $p > 0.05$), while MNE didn't show any antiinflammatory activity. The MEE oral preparation showed good antiinflammatory effect at dose of 600 mg/kgBW. Mondokaki ethanolic extract gel (MEEG) which was applied topically showed statistically equal antiinflammatory effect with Na-diclofenac gel 1%, which concentration of 3% MEE showed better antiinflammatory effect. In conclusion, ethanol extract of Mondokaki plant had antiinflammatory effect when applied both orally and topically.

PROTECTIVE EFFECT OF POLYHERBAL FORMULATION ON ANTITUBERCULAR DRUGS INDUCED HEPATOTOXICITY IN RATS

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This study was designed to assess the protective effect of polyherbal formulation against antitubercular drugs induced liver toxicity. The polyherbal formulation contains extracts of *Justicia gendarussa*, *Tinospora cordifolia* and *Carica papaya*. The toxicity was induced by administration of antitubercular drugs (INH, RIF and Pyrazinamide) in rats pretreated with polyherbal formulation at different dose levels for 14 days p.o. Liv52 (2 mL/kg body weight) suspension was used as standard hepatoprotective formulation. Serum parameters like serum glutamate oxaloacetic transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), serum alkaline phosphatase (SALP), total protein (TPTN), total bilirubin (TB) and liver enzymes like catalase (CAT), sodium dismutase (SOD) and glutathione (GSH) were determined to evaluate the hepatoprotective activity of the polyherbal formulation. Wet liver weight, lipid peroxidation (TBARS method) and histopathological studies were other parameters used for evaluation. Treatment with polyherbal formulation led to significant amelioration of toxin induced changes in the biochemical parameters. The changes in biochemical parameters were almost normalised in the rats pretreated with polyherbal formulation and the activity was found to be comparable to that of Liv52. The above study concludes that, the polyherbal formulation has excellent hepatoprotective activity in antitubercular drugs intoxicated rats, which can be utilised to treat the hepatotoxicity induced by chronic administration of antitubercular drugs.

**PRELIMINARY STUDY OF ANTINOCICEPTIVE ACTIVITY OF
2,6-BIS-4-(HYDROXYL-3-METHOXYBENZYLIDINE)-
CYCLOHEXANONE, A CURCUMINOID DERIVATIVE, AND ITS
SUITABLE ROUTE OF ADMINISTRATION**

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The present study examined the antinociceptive activity of a curcuminoid derivative, 2,6-bis-4-(hydroxyl-3-methoxybenzylidene)-cyclohexanone or BHMC, using acetic acid induced abdominal constriction test model in mice. In this experimental model, pain was induced in mice through intraperitoneal injection with 0.6% acetic acid. The number of constrictions indicated the degree of pain perceived by the mice. Various concentrations of BHMC (0.03, 0.1, 0.3 and 1.0 mg/kg) were administered intraperitoneally or orally 30 minutes before acetic acid injection. Results showed that intraperitoneal administration of BHMC suppressed the number of abdominal constrictions in a dose dependent manner, with inhibition of 21.53%, 44.03%, 60.01% and 83.95%, respectively, while oral administration exhibited less efficacy in antinociceptive activity compared to intraperitoneal treatment, with inhibition of 10.39%, 25.52%, 34.71% and 33.23%, respectively.

**ANTIDIABETIC ACTIVITY OF SWIETENIA MACROPHYLLAE
(MELIACEAE) SEEDS IN NORMAL AND STREPTOZOTOCIN
INDUCED DIABETIC RATS**

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Swietenia macrophyllae (Meliaceae) commonly known as *tunjuk langit* in Malaysia is traditionally used to treat diabetes mellitus. However, literature review revealed very few reports on the evaluation of *S. macrophyllae* for antidiabetic activity. Therefore, this study was carried out to evaluate the antidiabetic and hypoglycemic effects of *S. macrophyllae* seed extracts. The seeds of *S. macrophyllae* were dried in an oven at 55°C for a week. The dried seeds were then ground into powder and subsequently extracted through maceration. Serial extraction method was carried out, using petroleum ether, followed by chloroform, methanol and finally with water. All the extracts were freeze dried and kept at 4°C prior to the experiment. Hypoglycemic and intraperitoneal glucose tolerance tests

(IPGTT) were adopted for antidiabetic studies. For hypoglycemic test, normal and streptozotocin-induced diabetic rats were used. The result showed that, none of the extracts had significant effect on the glucose level of normal rats. However, in diabetic rats, the aqueous extract was able to reduce glucose level significantly ($p < 0.05$) compared to control at 3, 5 and 7 hours after administration of the extract. For IPGTT on normal rats, the results showed that petroleum-ether extract was significantly ($p < 0.05$) able to reduce blood glucose level as compared to the control. The present study confirmed that *S. macrophyllae* seed extract possesses a potential antidiabetic activity. Further study is on going to isolate the active chemical constituents responsible for the antidiabetic activity.

THE ANTIULCEROGENIC EFFECT OF FLAVOKAWIN B, ZERUMBONE AND BHMC ON HCL/ETHANOL INDUCED MICE

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Gastric ulcer is a common disorder where discontinuity in the gastric mucosa is observed. It is caused by many factors like stress, drugs, alcohol and is reported to be due to an imbalance between offensive acid-pepsin secretion and defensive mucosal factors. The conventional drugs used in the treatment of gastric ulcer contribute various undesirable side effects and drug interactions. The objective of this study is to evaluate the effect of Flavokawin B and Zerumbone compounds on HCl/ethanol induced gastric ulcer in experimental mice. Mice were divided into groups of 6 animals each that were fasted 24 h prior to receiving an oral dose of the vehicle; saline (negative control - 10 mL/kg), ranitidine (positive control - 100 mg/kg), Flavokawin B and Zerumbone (100, 50 and 10 mg/kg body wt.). After 1 h, all groups were treated orally with 0.3 mL of a 1M HCl/60% ethanol solution (HCl/ethanol) for gastric ulcer induction. Animals were killed 1 h after the administration of HCl/ethanol, and the stomachs were excised, sum of length of lesions (mm) were calculated and sum of all lesions index were determined. From this study, significant reduction in lesion index was observed in ulcer induced animals treated with Flavokawin B and Zerumbone compounds compared to negative control mice (ulcerated mice). In future, this project could be able to explore a new concept of using Flavokawin B and Zerumbone compounds as an antiulcer agents instead of other existing remedies.

ANTINOCICEPTIVE ACTIVITY OF *ACMELLA ULIGINOSA* HEXANE FRACTION

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The hexane fraction of crude methanol extract from *Acmella uliginosa* (Asteraceae), was evaluated for its antinociceptive activity in mice by using chemical and thermal models of nociception using acetic acid-induced abdominal writhing, formalin-induced paw licking and hot plate tests. The HFAU (p.o.) at doses of 3, 10, 30 and 100 mg/kg produced significant dose-dependent inhibition in the acetic acid-induced abdominal writhing test as compared to the control. In the formalin-induced paw licking test, the HFAU also significantly reduced pain in both neurogenic and inflammatory phases at all doses. However, HFAU was found to inhibit inflammatory pain better than neurogenic pain at all doses, especially at 100 mg/kg. Significant increase in baseline was observed after oral administration of HFAU at all doses when compared with control group in the hot plate test. Thus, these results suggest that the HFAU possesses antinociceptive activity at both central and peripheral levels, and thus supports its folkloric use as an analgesic.

ANALGESIC EFFECT OF SIDAGURI PLANT EXTRACTS (*SIDA RHOMBIFOLIA* L.) IN THERMALLY-INDUCED PAIN IN MICE

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Traditional medicines derived from plants have been used as an alternative treatment to treat pain, due to the side effects of synthetic drugs. One of the plants that has long been used by society for this purpose is the sidaguri plants (*Sida rhombifolia* L.). The aim of this study was to evaluate the pharmacological analgesic activity of sidaguri plants given orally. This research was conducted in an experimental study by complete randomised design. This study used mice as subjects, the hot plate as pain inducer, with antalgins as a standard synthetic analgesic agent. Sidaguri plant extracts were prepared by percolation with ethanol (EES), *n*-hexane (En-HS), and ethyl acetate (EEAcS). The data obtained were statistically tested using ANOVA. The results showed that the EES have analgesic activity similar to that of antalgins at the dose of 100 mg/kg BW ($n = 6$, $p > 0.05$). On the other hand En-HS and EEAcs were found not to have any analgesic activity. EES showed good results at a dose of 400 mg/kg BW as analgesics.

ANTIOXIDANT PROPERTIES OF RED DRAGON FRUIT (*HYLOCEREUS POLYRHIZUS*)

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Hylocereus polyrhizus is a plant belonging to the family Cactacea. In Asia, it is often called *dragon fruit* following its bright red skin with green overlapping fins covering the flesh. The aim of this study was to investigate total phenolic and flavonoid contents, and antioxidant activity of *H. polyrhizus* methanolic extract and its fractions. The flesh of the red dragon fruits were cut into small pieces and dried in an oven at 55°C. The dried flesh was then ground into powder and extracted with methanol using the maceration method. The methanol extract was then fractionated into chloroform, ethyl acetate, *n*-butanol and aqueous fractions using liquid-liquid partitioning. The total phenolic and flavonoid contents and free radical scavenging activity of *H. polyrhizus* methanolic extract and fractions were studied using Folin-Ciocalteu, aluminium chloride and DPPH spectrophotometric methods, respectively. The total phenolic content of the extract and fractions varied from 0.33% to 3.5% of dry weight, expressed as gallic acid equivalents (GAE). Among the extract and fractions, only ethyl acetate and chloroform fraction contains flavonoid compounds (0.91% and 0.34% of quercetin equivalents). The DPPH radical scavenging effects of the extract and fractions of *H. polyrhizus* increased in the order: ethyl acetate fraction > chloroform fraction > *n*-butanol fraction > methanol extract > aqueous fraction. With further data analysis, it was found that there was a correlation between the total phenolic content of the sample and its DPPH scavenging activity with correlation coefficient (*r*) being 0.697. These results suggest that phenolic compounds in this fruit provided substantial antioxidant activity.

INVOLVEMENT OF ATP-SENSITIVE K⁺ CHANNEL PATHWAY IN THE PERIPHERAL ANTINOCICEPTIVE INDUCED BY SYNTHETIC FLAVOKAWIN B IN MICE

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The possible participation of K⁺ channels in the antinociceptive action induced by Flavokawin B was assessed in the acetic acid-induced abdominal writhing test. Our previous findings showed that intraperitoneal administration of Flavokawin B produced significant dose-dependent antinociception in a similar test. In the present study, pretreatment of the mice with glibenclamide, (ATP-sensitive K⁺ channel inhibitors), charybdotoxin and apamin (large and small conductance Ca²⁺ activated-K⁺ channel

blockers, respectively), or tetraethylammonium (voltage-dependent K⁺ channel inhibitors) significantly reversed the Flavokawin B-induced antinociception. The results suggest that the peripheral antinociceptive effect of Flavokawin B may result from the opening of large and small conductance Ca²⁺-activated K⁺ channels, as well as ATP-sensitive K⁺ channels, which may cause hyperpolarisation of peripheral terminals of primary afferents.

ANTIOXIDANT EFFECT OF *PEPEROMIA PELLUCIDA* EXTRACTS

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Peperomia pellucida is a widely used traditional plant for treating inflammation, gout and arthritis and also for wound healing. The biological activities involved in the treatment are believed to be contributed by secondary metabolites synthesised in plants such as the phenolic compounds. Therefore, this research was carried out to determine the antioxidant activity and the phenolic content of various extracts of *P. pellucida*. Petroleum ether, chloroform and methanol were used serially to prepare three different extracts of the plant. The antioxidant study was performed using the DPPH free radical scavenging assay. Antioxidant activity revealed that petroleum ether and chloroform extracts of *P. pellucida* had a poor radical scavenging activity compared to the methanol extract. The free radical scavenging activity determined for petroleum ether and chloroform extracts were 0.829 ± 0.314 mg/mL and 0.160 ± 0.019 mg/mL, respectively. On the other hand, the free radical scavenging activity determined for methanol extract was 0.083 ± 0.008 mg/mL and its total phenolic content was 6.93%. The present study suggests that the methanol extract of this plant can be used as a potential antioxidant agent.

TOXICITY EVALUATION OF STANDARDISED 50% ETHANOL EXTRACT OF *ORTHOSIPHON STAMINEUS*

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The present investigation was carried out to evaluate the safety of standardised 50% ethanol extract of *Orthosiphon stamineus* (SEOS) by determination of its potential toxicity after acute and sub-chronic administration in rats. For acute toxicity study, up and down method (limit dose) was adopted. A single dose of 5000 mg/kg of the SEOS was given orally to 5 healthy Sprague-Dawley (SD) female adult rats. The rats were observed for mortality and clinical signs for 3 hours and then periodically for 14 days. For the sub-chronic toxicity study, the SEOS was administered orally at doses of 1250, 2500 and 5000 mg/kg per day for 28 days to female and male SD rats, respectively. The animals were sacrificed at the end of the experiment, followed by examination of their organs and blood serum. In the acute toxicity study, SEOS at a dose of 5000 mg/kg caused neither visible signs of toxicity nor mortality. All five rats survived until the end of observation period. Meanwhile in sub-chronic toxicity, administration of the standardised SEOS at 1250, 2500, and 5000 mg/kg for 28 days did not produce any mortality and there were no significant differences in the general condition, growth, organ weights, hematological parameters, clinical chemistry values, or gross and microscopic appearance of the organs from the treatment groups as compared to the control group. SEOS did not cause any death nor did it cause abnormalities in necropsy and histopathology findings. There were no acute or sub-chronic toxicity observed and this extract could be devoid of any toxic risk. The NOAEL for the SEOS is 3500 mg/kg per day for 28 days.

CYTOTOXIC EFFECTS OF *CRINUM AMABILE* EXTRACTS ON CANCER CELL LINES

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Cancer is one of the main causes of death worldwide including in Malaysia. Previously, reports showed that *Crinum* species have significant analgesic, antitumour and antiviral activity. Therefore, this experiment was undertaken to determine the cytotoxicity effects of various extracts of *C. amabile* against several cancer cell lines. In this study, MTS assay was chosen to evaluate the cytotoxic effects of various extracts of *C. amabile*. From the results, chloroform extract of *C. amabile* appeared to be the only extract that possessed cytotoxic

effect against the cell lines tested. Chloroform extract of *C. amabile* produced IC₅₀ values of 157.47, 105.59, 94.67 and 169.68 µg/mL against HCT-116, HT-29, MCF-7 and MDA-MB-231 cancer cell lines, respectively. While the other extracts (petroleum ether, methanol and water) showed no cytotoxicity to all the cell lines, at all the concentration tested (IC₅₀ values determined were > 200 µg/mL). Among the different cell lines tested, breast adenocarcinoma, MCF-7 appeared to be the most susceptible cell lines. The chloroform extract of *C. amabile* can be further studied for its cytotoxicity mechanism of action on this cancer cell line.

THE POTENTIAL OF BROMINATED SCHIFF BASES AS ANTIANGIOGENESIS AND ANTICANCER AGENTS

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Angiogenesis is the formation of new blood vessels from pre-existing host vasculatures stimulated by biochemical stimulators. Angiogenesis is involved in wound healing, embryonic development, and the female reproductive cycle, which is under elaborate regulations in the normal vascular system. However, malignant angiogenesis plays a critical role in cancer by being a normal delivering mechanism of oxygen and nutrients to the cells and tissues. As tumor angiogenesis caused by angiogenic inducers is the most critical factor in the growth of solid tumors, as well as their invasion and metastasis, early control of angiogenesis may be a promising therapeutic strategy for cancer. Schiff bases have been intensively investigated due to their antibacterial and anticancer properties. Three compounds of brominated Schiff bases, S4, S5, and S6 have been tested upon HCT-116 (human colon cancer), MCF-7 (human breast cancer), MDA-MB-231 (human breast cancer), and HUVEC (human umbilical vein endothelial) cell lines. All these three compounds showed significant activity on HCT-116 and HUVEC cell lines where the IC₅₀ values for the HCT-116 cell line are 81 µM, 86 µM and 76 µM, while for HUVEC cell line are 54 µM, 60 µM, and 58 µM, respectively. However, they were not toxic on MCF-7 and MDA-MB-231 cell lines. These three compounds also showed promising antiangiogenesis activity as they inhibited 100% of the rat blood vessel growth at 500 µM.

KOETJAPIC ACID INDUCES APOPTOSIS IN HUMAN COLORECTAL CANCER CELLS

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Sandoricum koetjape is a traditional plant belonging to the family Meliaceae. It is native to Southeast Asian countries, including Malaysia and the Philippines. In Malaysia, it is

locally known as *santol* and the bark is traditionally consumed as a tonic after giving birth. Koetjapic acid (KA) is a seco-A-ring oleanene triterpene isolated from *S. koetjape* Merr. In the present work, an attempt has been made to understand the cellular and molecular mechanisms of the potent cytotoxicity of KA towards human colorectal cancer cell line (HCT 116). Here we reported that KA induces apoptosis in HCT 116 cells, and eventually the induction of apoptosis was accompanied by activation of both extrinsic and intrinsic caspases. We were further motivated to investigate the pro-apoptotic properties of KA. The results showed that KA induces apoptosis by inducing nuclear fragmentation and condensation, and disruption in the mitochondrial membrane potential. Finally, early changes in 10 cancer-relevant genes were screened by cancer reporter gene array. KA down-regulates Wnt, HIF, MAPK/ERK/JNK, Myc/Max signalling pathways and causes simultaneous up-regulation of NF- κ B signalling pathway. Our results on apoptosis involving activation of caspase-3/7, 8 and 9 with concomitant down-regulation of pro-proliferative genes clearly demonstrated potent cytotoxic nature of KA that could be a promising chemotherapeutic agent.

ANTIANGIOGENESIS AND ANTIOXIDANT PROPERTIES OF *PARKIA SPECIOSA* HASSK. EXTRACTS

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Parkia speciosa Hassk is a traditional medicinal plant with strong antioxidant and hypoglycemic properties. This study aims to determine the total phenolic content and to investigate the antioxidant and antiangiogenesis properties of eight empty pods extracts from *P. speciosa*. The extracts showed high levels of total phenols with strong antioxidant effect by the DPPH scavenging assay. In rat aortic ring assay, the extracts inhibited the microvessels, outgrowth from aortic tissue explants by more than 50%. This activity was further confirmed by tube formation on matrigel matrix involving human umbilical vein endothelial cells. Cytotoxicity of the extracts was evaluated using XTT assay on endothelial cells as a model cell line of angiogenesis versus a panel of human cancer and normal cell lines. The extracts did not show acute cytotoxicity, but morphology examination of endothelial cells treated with *P. speciosa* extracts indicated induction of autophagy characterised by plenty of cytoplasmic vacuoles. Finally, the extracts were found to work by decreasing the expression of vascular endothelial growth factor by the endothelial cells. These results suggest *P. speciosa* as a good candidate for further studies including chemical profiling and in vivo antiangiogenesis evaluation.

EVALUATION OF *DATURA METEL* LINN. AGAINST BREAST AND COLORECTAL CANCER

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Datura metel Linn., a traditional medicinal plant belonging to the family Solanaceae is a poisonous herb that grows wild in the tropics. It is now being widely planted due to its chemical and decorative characteristics. In Malaysia, *D. metel* is locally known as *kecubung*, while the Chinese recognise it as *yáng jīn huā* and in other parts of the world it is also known as *datura*, devil's trumpet as well as raving nightshade. This plant is 1 of the 50 fundamental herbs in Chinese medicine. Traditionally, the Chinese have been using this herb to treat asthma; in which the dried leaves are rolled and smoked as a cigar. It has also been used for centuries in witchcraft rituals due to its hallucinogenic effects. The present work is aimed to evaluate the cytotoxic property of the methanolic extract of *D. metel* leaves against 2 isogenic human tumour cell lines namely, HCT116 derived from human colorectal cancer and MCF7 derived from estrogen dependent human breast cancer cells. The cell proliferation assay was performed using tetrazolium (MTT) method. The methanolic extract exhibited significant cytotoxicity against HCT116 cells with an IC₅₀ of 28.4 µg/mL. Similarly, it exerted potent cytotoxicity towards MCF7 cells (IC₅₀ of 28.77 µg/mL). These results highlight the potential of *D. metel* in the treatment of breast and colorectal cancer.

CYTOTOXIC AND ANTIANGIOGENIC ACTIVITY OF SUPERCRITICAL FLUID EXTRACTS OF *NIGELLA SATIVA* LINN

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Nigella sativa Linn. also commonly referred to as black cumin, is a popular spice that has been used since the times of the ancient Egyptians. In Islam, it is regarded as one of the greatest forms of healing medicine available as quoted by Prophet Muhammad; 'a medicine that can cure all illness except death'. Recent pharmacological findings highlights its potential role in amelioration of oxidative stress through free radical scavenging activity, the induction of apoptosis to thwart tumour growth, the reduction of blood glucose, and the treatment of rheumatic arthritis and diabetic blindness. It has also been cited to have potent immunostimulating and immunomodulating properties. Most of the diseases mentioned have strong involvement of angiogenesis, a process of new blood vessel development that plays a central role in tumour growth, rheumatoid arthritis, Alzheimer disease, diabetic blindness and age related macular degeneration. Recently we analysed the effect of the essential oil of *N. sativa* that was extracted by supercritical fluid

extraction using CO₂ (NSSCF) on angiogenesis. The NSSCF extracts were prepared by varying the pressure (3000, 4500 and 6000 psi) and temperature (32°C, 45°C and 60°C) of the extractor instrument. We found that NSSCF extract that was produced at 3000 PSI and 60°C inhibited neo-vascularisation in a 3D assay employing isolated rat aorta tissue by 80%. The extract did not cause any significant cytotoxic effect on the human umbilical vein endothelial cells (HUVEC). The result of this study favours the suggestion of NSSFE to be highly antiangiogenic and may be useful in the treatment or prevention of angiogenesis related ailments.

FLAVONOIDS CONTENT, TOTAL PHENOLIC AND ANTIOXIDANT ACTIVITY OF *VERNONIA AMYGDALINA* DEL

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Vernonia amygdalina, a member of the Asteraceae family, is a small shrub that grows in the tropical African and South East Asian countries and is widely used in the traditional treatment of many ailments. The aim of this study was to investigate the total phenolic and flavonoid contents, and the antioxidant activity of *V. amygdalina* methanolic extract and its fractions. The oven dried leaf of *V. amygdalina* was ground into powder and extracted with methanol using the soxhlet method. The methanol extract (ME) was then fractionated into chloroform (CF), ethyl acetate (EF), *n*-butanol (BF) and aqueous fractions (AF) using a liquid-liquid partitioning method. The total phenolic content, flavonoid content and free radical scavenging activity of *V. amygdalina* methanolic extract and its fractions were studied using Folin-Ciocalteu, aluminium chloride and DPPH spectrophotometric methods, respectively. The total phenolic content were found to be 15.6%, 9.4%, 7.6%, 6.5% and 2.8% mg gallic acid equivalents (GAE)/mg in EF, BF, ME, CF and AF, respectively. The EF exhibited the highest DPPH followed by BF, ME, CF and AF. The flavonoid content of the leaves extract of *V. amygdalina* were mainly quercetin which ranged from 0.02 to 0.36 mg/1 g quercetin, with the highest level found in EF (4.5%), followed by BF (4.4%) and AF (0.38%). With further data analysis, it was found that there was a significant correlation ($p < 0.05$) between the total phenolic content of the sample and its DPPH scavenging activity with correlation coefficients (r) of -0.907. These results suggest that phenolics in the plant were mainly responsible for its antioxidant activity.

ANTIHYPERGLYCEMIC AND HYPOGLYCEMIC ACTIVITY OF FOUR EXTRACTS OF *FICUS DELTOIDEA* (MORACEAE) LEAVES ON NORMAL RAT

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Ficus deltoidea (Moraceae), known as *mas cotek* in Malaysia is widely used in folk medicine to reduce blood sugar and cholesterol levels. The aim of this experiment is to study the antihyperglycemic effect of *F. deltoidea* extracts. *F. deltoidea* leaves were dried in an oven at 45°C and the dried leaves were ground into powder and extracted serially with chloroform, methanol and water by the maceration method. The extracts were concentrated by using rotary evaporator and lyophilised by freeze drier. Lyophilised extracts were dissolved in normal saline and administered into the over-night fasted normal male Sprague Dawley (SD) rat for hypoglycemic evaluation with Gliclazide as the reference drug, and for glucose tolerance test with metformin as the reference drug. Results of this study indicate 1.2 g/kg b.w. of aqueous extract of *F. deltoidea* possessed significant ($p < 0.05$) antihyperglycemic activity after one hour of administration. As aqueous extract of *F. deltoidea* leaves can lower blood glucose level in normal rats, it can be a potent antidiabetic drug but to reach this goal further studies need to be carried out to identify the compound responsible for this effect and probable mechanism of action.

PHARMACY

COMPARATIVE STUDY OF FERROUS SULPHATE PROVIDED IN ALGINATE CAPSULE AND GELATIN CAPSULE IN IRON DEFICIENCY ANEMIC PATIENTS

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Administration of enteric coated iron tablets and slow-release preparations results in fewer gastrointestinal side-effects, but less effective due to the release of iron beyond the optimal absorption site. The use of alginate capsule as a gastric delivery system to formulate ferrous sulphate is expected to have no gastrointestinal side effects and remain effective for the treatment of anemia. The aim of this study was to compare the effects of ferrous sulphate given in alginate and gelatin capsules to increase haemoglobin and ferritin levels in iron deficient anemic patients. Study was conducted in a randomised, double blind, and controlled manner. Ferrous sulfate in gelatin capsule was used as control. Ferrous sulphate dose was 300 mg (~ 60 mg Fe), taken once a day an hour before meals for 4 weeks. Baseline characteristics of subjects (age, Hgb and serum ferritin level) did not differ significantly. At the end of the fourth week, haemoglobin and serum ferritin level were measured. The increase of the average haemoglobin level in gelatin and

alginate capsule groups were $0.46 \text{ g/dL} \pm 0.57 \text{ g/dL}$ and $0.51 \pm 0.46 \text{ g/dL}$, respectively. The increase of serum ferritin level in the group of gelatin and alginate capsule were $29.28 \pm 18.9 \text{ } \mu\text{g/L}$ and $16.68 \pm 12.95 \text{ } \mu\text{g/L}$, respectively. Both of these haematological parameters did not differ significantly in both groups based on independent samples T-test ($p > 0.05$). Based on these results, it was concluded that the 300 mg ferrous sulfate in alginate capsules gave equivalent therapeutic effect as gelatin capsules.

PRESCRIBING PATTERN OF OBSTRUCTIVE AIRWAY DISEASE MEDICINES IN OUTPATIENT CLINICS AT A TERTIARY CARE HOSPITAL

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In Malaysia, drugs for obstructive airway diseases (OADs) are among the top 10 in the list of high distribution of expenditure by therapeutic groups. This retrospective study was to determine the prescribing pattern of drugs for OADs in outpatient clinics at Hospital Tengku Ampuan Rahimah (HTAR), a tertiary care hospital. Post ethics approval, data were collected by screening all outpatient prescriptions in May, June and August 2008 and were then recorded and analysed descriptively. Overall, there were 548 prescriptions containing OAD medications [May: $n = 182$ (33.21%); June: 162 (29.56%); August: 204 (37.23%)]. Prescribing frequency of OAD drugs was high in August (243) followed by May (231) and June (204). Metered dose inhaler was highly prescribed (50.44%) followed by dry powder inhaler (12.53%) and tablet (5.90%). The frequency of prescribed combined inhaler of long acting β_2 -adrenergic agonists with corticosteroids was relatively small in number (6.93%). The number of patients treated with short acting β_2 -agonists decreased slightly from May to June. The prescribed percentage of theophylline was very small (0.15%). Montelukast sodium (4.87%) was also prescribed to OAD patients albeit not being stated in the Malaysian's clinical guideline of asthma and chronic obstructive pulmonary disease. The results may reflect the pattern of pharmacotherapeutic management for OAD patients and the number of prescriptions with OAD drugs provided a crude estimate of OADs prevalence at HTAR. Overall, the prescribing pattern of OAD may help the pharmacy department in drugs and budget allocation for the next term's procurement.

ADVERSE DRUG REACTION REPORT IN A TERTIARY CARE HOSPITAL

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ADR is the 'response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological function'. The study was asset to number of cases of ADR from 2005 to 2009 at Hospital Selayang, a tertiary care hospital. A retrospective study was done from 23 February 2010 until 10 March 2010 to collect data of drugs reported as causing ADR from the data system, soft copy reports of ADR and the Selayang Hospital Bulletin. Data on the ADRs report were evaluated to understand the pattern of the ADRs with respect to patient demographics, number of prescribed drugs, nature of the reactions, characteristics of the drugs involved, and outcome of the reaction. Total of ADRs cases reported were 993 cases. The highest case reports was 335 (33.73%) and the lowest case reports was 120 (12.08%) in 2009 and 2008, respectively. The highest cases reported, 472 cases (47.53%) were from the Dermatology Department whereas the lowest cases reported, 47 (4.73%) were from the Emergency Department. The mean was 199 cases, reported each year. The top 10 drugs were reported in 2008 and 2009. Cefuroxime and cloxacillin were the highest (13.88%) and ampicillin was the lowest (5.55%) cases reported in 2008 whilst split virion, inactivated, adjuvanted were the highest (35.24%) and meropenem was the lowest (4.91%) cases reported in 2009. Percentages were found out among prescription drugs and complementary drugs in 2008 and 2009. 77% prescription drugs and 23% complementary drugs causing ADRs were calculated in 2008, while 94% prescription drugs and 6% complimentary drugs causing ADRs were found in 2009.

KNOWLEDGE ASSESSMENT OF ASTHMA AMONG PHARMACY STAFF IN A TERTIARY CARE HOSPITAL

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Adequate current knowledge on asthma is an added value to better therapeutic management. The study was to evaluate the level of knowledge on asthma among pharmacy staffs at Hospital Selayang, a tertiary care hospital. The adapted self-administered 18-item questionnaires were directly disseminated, collected and descriptively analysed. Scoring level of the respective knowledge was defined as poor (0-4), moderate (5-9), good (10-14) and excellent (15-18). Total respondents were 56 staffs including pharmacists (50%), pharmacist assistants (26.8%) and others (23.2%). Socio-demographic data of respondents include: 67.9% female, 73.0% within the age range of 20-29 years old, 69.6% Malays, and 82.1% completed higher education level (college/universities). Regarding the duration of hospital working-year, 48.2%, 21.4%, 17.9%, 8.90% and 3.60% of the respondents worked ≤ 1 year, 2-3 years, 4-7 years, 8-5 years and ≥ 16 years, respectively. About 46.4% of respondents were involved in counseling sessions and 60.71% have no family history of asthma. Overall, the study exemplified excellent knowledge level with respect to (i) gender: 35.71% females and 14.29% males; (ii) educational background: 46.43% of college/university graduates; (iii) post: 39.29% pharmacists, 7.14% pharmacist assistants, and 3.57% others; (iv) duration of working: 19.64% ≤ 1 year, 16.07% 2-3 years, 8.93% 4-7 years and 5.36% 8-15 years (3.57% with working experience of ≥ 16 years scored good); (v) 37.5% and 12.5% that were involved and not involved in counseling session, respectively; and (vi) 33.93% and 16.07% without and with family history of asthma, respectively. None demonstrated poor knowledge level on asthma.

PATTERN OF PRODUCT RECALL IN A TERTIARY CARE HOSPITAL: 2003-2009

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Decision for product recall (PR) is made if there is or may be risk to the user of the product due to faulty production or medical reasons. This retrospective study was to evaluate the pattern of PR incidences in Hospital Tengku Ampuan Rahimah (HTAR). Data in PR forms between January 2003 and December 2009 were recorded and analysed descriptively. Overall in 7 consecutive years, HTAR received 74 general nation PR notices [2003: n = 17 (23%); 2004: 14 (19%); 2005: 12 (16%); 2006: 3 (4%); 2007: 5 (7%); 2008: 16 (22%); 2009: 7 (9%)]. About 27 (36%) of direct PR notices involved HTAR merely. National Pharmaceutical Control Bureau issued 7% of the PR notices, 92% from companies voluntarily and 1% is unstated. Pharmaniaga Manufacturing requested the highest PR (16%), followed by Safire Pharmaceuticals (14%), Duopharma (12%) and SM Pharmaceuticals (12%). Degree III was the commonest action level of nation PR (78%) compared to degree I (3%). Among the reasons of PR include physical appearance (41%), physicochemical parameter (28%), adverse drug reaction (4%), microbial test (4%), packaging (4%), contamination of foreign particles (3%), mixed up with other ingredients (3%) and sterility (1%). The most respective frequent dosage form was tablet (51%), followed by injection (15%) and suspension (12%). The response periods toward PR were: 39% < 7 days, 38% > 7 days- < 1 month, and 16% > 1 month. Essential actions taken by all respective parties in dealing with the specification of the pharmaceutical products ensures harmless drug use hence averting possible health risks to patients.

METHADONE MAINTENANCE THERAPY: EVALUATION ON OUTCOME

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This is a cross-sectional study evaluating the clinical and social outcomes of patients attending the Methadone Maintenance Therapy (MMT) Clinic of the Psychiatry Department of Hospital Tengku Ampuan Rahimah, Klang between 2nd February 2010 and

1th April 2010. Examples of clinical outcomes observed are abstinence to substance abuse and free of withdrawal side-effects while employability and family support are for social outcomes. Both descriptive and quantitative analyses (ANOVA) are used for analysis. Forty adult patients with a mean age of 41.90 ± 9.61 years and are on treatment for at least 1 year are selected as obtained from the patients' records. Inter-ethnic distribution was Malay 60%, Chinese 30%, and Indians 10%. Mean duration of therapy was 107.99 ± 31.36 weeks. The mean age of being a drug abuser was 22.22 ± 6.81 and 18 (45%) clients started substance abuse between 13–20 years old. 75% were hepatitis positive, 3 were HIV positive and most had history of intravenous substance use. 52.5% of the clients had abnormal liver function associated with hepatitis. 57.50% of urinalysis for drug abuse after 6 months of therapy were negative. Clinical data on HIV, hepatitis C and liver function showed a high rate of HCV accompanied with impaired liver function among the MMT patients. Based on the levels of drug dependency the initial starting daily dose of methadone was 20 mg and the highest maintenance dose was 130 mg. Adherence rate during the last 1 year was 87%. Sleepiness (47.5%) and constipation (35%) were the side effects reported. No significant difference on illicit drug use and duration of therapy and IVU was strongly associated with hepatitis virus ($p < 0.05$). The number of employed patients from baseline has increased after 1 year of treatment ($p < 0.05$). Finally this study managed to highlight some of the social and clinical factors that contribute to the successful implementations of MMT among drugs abusers in Malaysia.

DRUG USE EVALUATION OF CIPROFLOXACIN FOR WARD HOSPITALISED PATIENT IN ONE OF BANDUNG'S PRIVATE HOSPITAL, INDONESIA

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Ciprofloxacin is a broad spectrum drug from a quinolone derivative. It is used wide spread clinically. A drug use evaluation of ciprofloxacin in ward hospitalised patients based on physician prescriptions written within January–March 2006 in one of the private hospital in Bandung has been completed. The evaluation was conducted using retrospective method with determined criteria such as the diagnostic accuracy or rational therapy and drugs interaction. A retrospective drug-utilisation review was carried out by checks from medical records after medication from ward hospitalised patients. Medical records contains drugs dispensed from physician prescriptions, usually to check claims data to identify potentially inappropriate prescriptions for individual patients. The evaluation has been observed from 463 prescriptions consisting of men at 49.46% and women at 50.54%. Observation results showed non-generic drug use at 7.06% and generic drug use at 28.94%, length of therapy medicinize faction of ciprofloxacin at most between 1–4 days (46.65%) and fewest more than 7 days (16.42%). There were 23.97% interaction case medicine faction of ciprofloxacin with other drug which have pharmacology interaction (6.05% pharmacodynamic interaction and 17.92% pharmacokinetic interaction).

Combination case medicize faction of ciprofloxacin with other drug was 4.54% for synergistic combination and 2.36% for antagonistic combination.

**PRESCRIBING PATTERN OF ANTIDIABETIC AGENTS:
EXPERIENCE OF OUTPATIENT CLINICS IN A HOSPITAL AT
KLANG VALLEY**

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Diabetes mellitus (DM) is one of the major health problems in Malaysia with escalating prevalence every year hence increasing the expenditure of the healthcare system. This retrospective study was to investigate the prescribing pattern of antidiabetic (AD) drugs in outpatient clinics at Hospital Tengku Ampuan Rahimah (HTAR), a tertiary care government hospital. Post ethics approval, data were collected by screening all outpatient prescriptions in May, June and August 2008 and were then recorded and analysed descriptively. Where applicable, ANOVA and t-test were used with a *p* value of < 0.05 indicating significant differences. Overall, there were 2551 prescriptions containing AD medications out of 46267 (mean per day = 746 prescriptions) of total prescriptions. The average of total AD prescriptions per day was 41 prescriptions that contributed to 5.5% of total prescription at outpatient clinics per day. Oral hypoglycaemic agents were highly prescribed (n = 2991, 74.2%) compared to insulin (n = 1042, 25.8%) significantly (*p* < 0.05). About 69.3% of diabetic patients received pre mixed insulin (Mixtard® > Monotard® > Humulin 70/30®). Rapid acting insulin (21.5%) was more likely to be prescribed followed by intermediate acting (7.0%) and long acting insulin (2.2%). Metformin was the significant AD drugs of choice (44.8%), followed by gliclazide (30.4%), glibenclamide (15.6%), acarbose (7.7%) and metformin-glibenclamide (1.6%). The study revealed the prescribing practices of AD that adhere to the Malaysian clinical practice guidelines of DM. Pharmacy department may plan the budget and drugs allocation to ensure diabetic patients receive their respective AD drugs with essential adherence towards therapy and blood sugar control.

**PROBLEMS OF ANTIBIOTIC USE IN SEPSIS PATIENT:
A PROSPECTIVE OBSERVATIONAL STUDY IN ONE OF
YOGYAKARTA STATE HOSPITAL, INDONESIA**

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Sepsis is a systemic infection that potentially leads to complications and death. Problems of antibiotic use in sepsis patient are increase in morbidity, mortality and antibiotic resistance. The objective of this study was to determine types and quantity of drug related problems (DRPs) in antibiotic use in sepsis patients. A prospective observational study was conducted on September until November 2008 at the internal medicine ward in one of Yogyakarta's state hospital. The population of the study was hospitalised adult patients who met the criteria for sepsis syndrome. The observations included three categories of antibiotic use problems such as indication, antibiotic selection and inappropriate dose of antibiotic. The problems of antibiotic use were based on the selection of empirical antibiotic in sepsis, evidence based medicine in sepsis and discussion with clinical pharmacist and doctor to seek their opinion. 26 admitted patients were evaluated. The DRPs were identified in 23 patients comprising of 67 cases; indications (35 cases), inappropriate antibiotic (26 cases) and inappropriate dose of antibiotic (6 cases). Twenty four types of antibiotics were evaluated, of which ceftriazone (26 patients) were found to be the most frequently used antibiotic in evaluated patients. This observation provides an insight about the use of antibiotic in sepsis patient. There is a need for an antibiotic guideline based on the local antibiotic resistance pattern as well as a collaborative effort from all the health care professionals.

BIOLOGY

**EFFECTS OF THIOL COMPOUND SUPPLEMENTATION DURING
IVM ON SUBSEQUENT BOVINE EMBRYO DEVELOPMENT**

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The addition of low molecular weight thiol compounds such as cysteamine and β -mercaptoethanol (β -ME) during in vitro maturation (IVM) has been found to increase intracellular glutathione (GSH) synthesis and consequently improving embryo development and quality. The increase in intracellular GSH concentration during IVM

provides bovine oocytes with a large storage of GSH, available for protection against oxidative damage during subsequent embryo development until the blastocyst stage. Slaughterhouse oocytes (n = 664) were used to study the effects of manipulating the culture's micro-environment condition by supplementing the maturation medium with 200 μ M cysteamine or 200 μ M β -ME on embryo development to blastocyst stage. Analysis of variance and Duncan's multiple range test were used to test the significance of the parameters measured at $p < 0.05$. The results of the present study showed that the addition of cysteamine and β -ME in the IVM medium improved the development of bovine embryo to the blastocyst stage. Grades A (36.69% and 22.32%) and B (33.84% and 26.09%) oocytes showed higher blastocyst rate in cysteamine or β -ME modified micro-environment, respectively, compared to the oocytes in the control group (Grade A = 19.48% and Grade B = 15.44%). This condition may provide oocytes with favourable intracellular conditions to support maturation, fertilisation and subsequent embryo development in vitro. In conclusion, the supplementation of these thiol compounds during IVM improved the maturation efficiency of oocytes by increasing glutathione content, hence, enhancing embryo development and resulting in more embryos reaching the blastocyst stage.

**ANTIBACTERIAL ACTIVITY OF EXTRACT AND FRACTIONS
FROM NIMBA LEAF (*AZADIRACHTA INDICA* A. JUSS) TO
ESCHERICHIA COLI AND *STAPHYLOCOCCUS AUREUS* BACTERIA**

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The phytochemical screening of Nimba leaf indicated the presence of glycoside, flavonoid, tannin and steroid/triterpene. The extraction of plant simplex was first done by maceration using n-hexane and then the residue was extracted by ethanol. The antibacterial activity test was performed in vitro by agar diffusion method using punch hole toward *Escherichia coli* and *Staphylococcus aureus* bacteria. The examination of antibacterial activity from n-hexane extracts toward *S. aureus* did not show growth inhibition, but showed growth inhibition on *E. coli* with minimum inhibitory concentration of 70 mg/mL. The examination of antibacterial activity from ethanol extract showed inhibition on the growth of *E. coli* and *S. aureus* with minimum inhibitory concentration of 10 mg/mL and 30 mg/mL, respectively. Ethanol extract was fractionated by vacuum liquid chromatography with ethyl acetate and ethanol as the solvents. The result of vacuum liquid chromatography produced 11 fractions and pooled to 8 fractions (F1-F8) after thin layer chromatography with ethanol:ethyl acetate (8:2) as mobile phase, and silica gel 60 GF254 as the stationary phase. Fractions F1-F4, F6-F7, F5 and F8 inhibited growth of *E. coli* with minimum inhibitory concentration of 7 mg/mL, 6 mg/mL, 50 mg/mL whilst for *S. aureus* were 8 mg/mL, 7 mg/mL, 50 mg/mL, respectively.

ANTIBACTERIAL AND ANTIFUNGAL ACTIVITIES OF CYMBOPOGON NARDUS ESSENTIAL OIL

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Essential oils and their components are becoming increasingly popular as naturally occurring antimicrobial agents. In this study the chemical composition and antimicrobial activity of *Cymbopogon nardus* essential oils were determined. The essential oil components which were identified by GCMS analysis are as follows: β -terpinyl acetate, isopulegol, *cis*-geraniol, citronellyl formate, *L*- β -pinene, δ -cadinene, γ -elemene and seychellene. The minimum inhibitory concentration (MIC) of essential oils against a few selected pathogenic bacteria (*Staphylococcus aureus* ATCC 25923, *Bacillus anthracis* ATCC 14578, *Pseudomonas aeruginosa* ATCC 27853 and *Escherichia coli* ATCC 35218) and fungi (*Candida albicans* ATCC 10231 and *Cryptococcus neoformans* ATCC 90112) were determined using disc diffusion method. The essential oils showed slightly potent inhibitory effects with mean diameter of inhibition zones ranging from 7.5 mm to 9.0 mm. Similar results were also obtained for the fungi, where the essential oils showed inhibitory effects with slightly wider diameter of inhibition zones which ranged from 7.8 mm to 12.0 mm. All microorganisms showed sensitivity towards *C. nardus* except for *P. aeruginosa*. The MIC values against these microorganisms ranged from 4.69 mg/mL to 37.5 mg/mL. The findings thus indicate the possibility of exploiting *C. nardus* essential oil as an effective inhibitor for the growth of some pathogenic microorganisms in the field of medicine.

MEDICINAL PLANTS OF TOBA PLATEAU, NORTH SUMATERA, INDONESIA

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Several species of highland plants are utilised as medicinal plants by the local Batak community. Among these medicinal plants, four species are popularly used by the local community. The identified four species are *Pinus merkusii*, *Ficus deltoidea*, *Lantana camara* and *Ananas comosus*. Essential oil from *P. merkusii* has been widely used from skin treatments to cancer. *P. merkusii* populations are recorded growing well in the dried sites. *F. deltoidea* (*mas cotek*) has been used for controlling blood pressure, and as an aphrodisiac. Local people used *L. camara* for curing tuberculosis (TB), rheumatism, abscess and bruise. Good growth of *L. camara* populations are found at mining zones, agriculture areas and secondary forests. *A. comosus* (pineapple fruit) has been used for the treatment of gastric, as an antimononucleosis and diuretic and for cleaning skin debridement. The plant populations are found at agriculture areas that are cultivated by local people commercially.

A WEED SPECIES, *LIMNOCHARIS FLAVA* USED AS TRADITIONAL MEDICINE

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This article presents a summary of research findings on *Limnocharis flava* as a source of medicine and food. *L. flava* (*paku rawan*) is a noxious aquatic weed in paddy fields but is edible. In Balik Pulau, the weed populations have invaded most parts along the ecotone between rice fields and roads. The invading sites are generally high in water level. There are a number of studies on this weed that reports its antioxidant properties. In addition, the weed also contains nutritive dietary sources such as carbohydrate, gross calorific value, ash, crude fat, crude fibre, crude protein, vitamin C, potassium, calcium, copper, magnesium, zinc, nitrogen, iron and β -carotene. These properties are able to improve the appetite, digestive system and increase availability of nutrient in body to maintain our health.