# LIST OF PUBLICATIONS AND ABSTRACTS YEAR 2017

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<td>Amin OS. Malignant middle cerebral artery infarction. <em>BMJ Case Reports</em>, 2017; doi:10.1136/bcr-2016-219117. (CiteScore: 0.13; Tier: Q3).</td>
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<td>Amin OSM, Mahmood MM. Simultaneous left-sided hypertensive putaminal and thalamic haemorrhages. <em>BMJ Case Reports</em>, 2017; published online. doi:10.1136/bcr-2017-219300. (CiteScore: 0.16; Tier: Q4).</td>
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<td>Wong SF, Lim PKC, Mak JW, Ooi SS, Chen DKF. Molecular characterization of culturable bacteria in raw and commercial edible bird nests (EBNs). <em>International Food Research Journal</em>, 2017; (in press). [SRAS funded project]. (CiteScore: 0.93; Tier: Q3).</td>
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Rodent models of glaucoma and their applicability for drug discovery

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Abstract
Rodents have widely been used to represent glaucomatous changes both in the presence and absence of elevated intraocular pressure (IOP) as they offer clear advantages over other animal species. IOP elevation is commonly achieved by creating an obstruction in the aqueous outflow pathways, consequently leading to retinal ganglion cell and optic nerve (ON) damage, the hallmark of glaucoma. These changes may also be achieved in the absence of elevated IOP by directly inflicting injury to retina or ON. Areas covered: This paper presents a summary of currently used rodent models of glaucoma. The characteristics of these models from several studies are summarized. The benefits and shortcomings of these models are also discussed. Expert opinion: The choice of animal model that closely represents human disease is key for successful translational of preclinical research to clinical practice. Rodent models of rapid IOP elevation are likely to be least representative, whereas models such as steroid-induced glaucoma models more closely resemble the trabecular meshwork changes seen in glaucomatous human eyes. However, this model needs further characterization. Rodent models based on direct retinal and ON injury are also useful tools to investigate molecular mechanisms involved at the site of final common pathology and neuroprotective strategies.

Keywords: Glaucoma models, intraocular pressure, optic nerve, retinal ganglion cells, rodents.
Targeting ECM remodeling in disease: Could resveratrol be a potential candidate?

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Abstract
Disturbances of extracellular matrix homeostasis are associated with a number of pathological conditions. The ability of extracellular matrix to provide contextual information and hence control the individual or collective cellular behavior is increasingly being recognized. Hence, newer therapeutic approaches targeting extracellular matrix remodeling are widely investigated. We reviewed the current literature showing the effects of resveratrol on various aspects of extracellular matrix remodeling. This review presents a summary of the effects of resveratrol on extracellular matrix deposition and breakdown. Mechanisms of action of resveratrol in extracellular matrix deposition involving growth factors and their signaling pathways are discussed. Involvement of phosphoinositol-3-kinase/Akt and mitogen-activated protein kinase pathways and role of transcription factors and sirtuins on the effects of resveratrol on extracellular matrix homeostasis are summarized. It is evident from the literature presented in this review that resveratrol has significant effects on both the synthesis and breakdown of extracellular matrix. The major molecular targets of the action of resveratrol are growth factors and their signaling pathways, phosphoinositol-3-kinase/Akt and mitogen-activated protein kinase pathways, transcription factors, and SIRT-1. The effects of resveratrol on extracellular matrix and the molecular targets appear to be related to experimental models, experimental environment as well as the doses.

Keywords: Resveratrol, extracellular matrix, matrix metalloproteinases, TGF-β.
Ahmad AA, Ikram MA. Plating of an isolated fracture of shaft of ulna under local anaesthesia and periosteal nerve block. A Case Report. Trauma Case Reports, 2017; 12: 40-44. (CiteScore: 0.11; Tier: Q4).

Plating of an isolated fracture of shaft of ulna under local anaesthesia and periosteal nerve block. A Case Report

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Abstract
Isolated fractures of shaft of ulna are common. Plate fixation with anatomic reduction is thought to produce the best functional results in closed or open fractures. Surgery can be done under general and various types of regional anaesthesia. We report a case of fracture shaft of ulna treated by plating under a combination of WALANT (wide awake, local anaesthesia, no tourniquet) using tumescent anaesthesia and periosteal nerve block as a day care procedure.

Keywords: Plating of ulna, Periosteal block, WALANT.

**Implementing professionalism by deprofessionalized strategies: A moral quandary**

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**Abstract**

Monetary fine proceedings has been one of the methods of upholding professionalism amongst health care professionals. Professionalism as a concept is multifaceted and fragmented and it has become symbolic to the extent that, unfortunately, some traits of professionalism showcase the whole concept. It seems fair to interpret the symbolic views on the concept of professionalism as means to capitalize on certain aspects of professions such as commercial profitability for the employer and respected status for the profession. Evaluation of professionalism is often implicit and inadequate; and assessing professionalism by relying on abstract and idealized definitions implies that professionalism is a compounded composite of certain set of stable traits. We suggest to refer to the theory of values-based practice so as to achieve collocated views on professionalism among employers and health academics. Instead of capitalizing on certain traits of professionalism to project the whole concept of professionalism, we may need to relook at the traits of professionalism as values. It is extremely crucial to internalize the values of the health profession in the future health professionals, so that the future health professionals imbibe the professionalism through dialog and democratic methods of sharing values during the course of professional development.

**Keywords:** Professionalism, Deprofessionalization, Health care students.

**Evaluation of patient satisfaction with HIV/AIDS care and treatment: A cross-sectional study**

Syed Imran Ahmed, Ashvinni Ramach, Keivan Ahmadi, Syed Shahzad Hasan, Christopher KC Lee.

**Abstract**

**Background, aims and objectives:** Patient experience influences the adherence to therapy and achievement of treatment outcomes, supplementing traditional indicators such as care processes and survival outcomes. This study aimed to examine the effect of relationship with healthcare providers on patient satisfaction.

**Methods:** A cross-sectional study carried out at an HIV outpatient clinic from August 2013 to October 2013. Patients were interviewed using a questionnaire adapted and contextualised from an online database. The questionnaire covered aspects related to healthcare providers’ attitude and knowledge, clinic services, patient autonomy and dignity, characteristics of healthcare providers as well as the sociodemographic backgrounds of the participants. A R® program for statistical computing was used for data analysis.

**Results:** Satisfaction with healthcare providers and respect for patient autonomy contributed the most to overall patient satisfaction, influencing 35% of the observed variance in patient responses. Clinic services and independent characteristics of healthcare providers also had minor roles in influencing patient experience. Social components outweighed clinical components in terms of sociodemographic influence on perceived quality of care. Education levels ($p \leq 0.05$) and employment status ($p \leq 0.1$) were significant determinants of patient experience; however, they were the only two sociodemographics associated with patient satisfaction. Other social and all clinical factors were not significantly associated with patient experience.

**Conclusion:** Relationship with healthcare providers as well as the degree to which patient autonomy is maintained are the most important determinant of patient satisfaction. Overall, social components have more prominent roles in influencing patient satisfaction compared to clinical components.

**Keywords:** HIV/AIDS, patient characteristics, patient satisfaction, person-centered healthcare, quality of care, socioeconomic status.

Attitudes and barriers towards HIV screening: A qualitative study of people living with HIV/AIDS (PLWHA) in Malaysia

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Abstract

Background: Understanding patients’ perspective towards HIV screening in Malaysia is pivotal to explore challenges faced by these individuals. This would be beneficial for developing local plans to improve the health-seeking behaviours among population at risk of HIV/AIDS.

Methods: A qualitative research methodology was adopted to explore HIV/AIDS patients’ views about disease screening. A semi-structured interview guide was used for in-depth patient interviews. All interviews were audio-recorded and were subjected to a standard content analysis framework for data analysis.

Results: Most patients were positive about screening and the value of knowing about their status early. However, fear of social stigma, discrimination, lack of support system and lack of public understanding were identified as major concerns affecting their willingness to be screened. They were concerned about mandatory screening being implemented without improvement in support system and public education.

Conclusions: Reluctance to seek HIV screening is an important factor contributing to transmission in developing countries. In the Malaysian context, efforts should be made to strengthen screening strategies especially in the most-at-risk populations to monitor the epidemic and target prevention strategies.

Practice implications: In a multicultural context, HIV preventive strategies must include disease awareness, including measure to tackle barriers towards screening.
Graphene-gold based nanocomposites applications in cancer diseases; Efficient detection and therapeutic tools

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Abstract

Early detection and efficient treatment of cancer disease remains a drastic challenge in 21st century. Throughout the bulk of funds, studies, and current therapeutics, cancer seems to aggressively advance with drug resistance strains and recurrence rates. Nevertheless, nanotechnologies have indeed given hope to be the next generation for oncology applications. According to US National cancer institute, it is anticipated to revolutionize the perspectives of cancer diagnosis and therapy. With such success, nanohybrid strategy creates a marvelous preference. Herein, graphene-gold based composites are being increasingly studied in the field of oncology, for their outstanding performance as robust vehicle of therapeutic agents, built-in optical diagnostic features, and functionality as theranostic system. Additional modes of treatments are also applicable including photothermal, photodynamic, as well as combined therapy. This review aims to demonstrate the various cancer-related applications of graphene-gold based hybrids in terms of detection and therapy, highlighting the major attributes that led to designate such system as a promising ally in the war against cancer.

Keywords: Graphene, Gold nanoparticles, Nanocomposite, Cancer, Detection, Therapy.

**Abstract**

Tengerensine (1), isolated as a racemate and constituted from a pair of bis-benzopyrroloisoquinoline enantiomers, and tengechlorenine (2), purified as a scalemic mixture and constituted from a pair of chlorinated phenanthroindolizidine enantiomers, were isolated from the leaves of *Ficus fistulosa* var. *tengerensis*, along with three other known alkaloids. The structures of 1 and 2 were determined by spectroscopic data interpretation and X-ray diffraction analysis. The enantiomers of 1 were separated by chiral-phase HPLC, and the absolute configurations of (+)-1 and (-)-1 were established via experimental and calculated ECD data. Compound 1 is notable in being a rare unsymmetrical cyclobutane adduct and is the first example of a dimeric benzopyrroloisoquinoline alkaloid, while compound 2 represents the first naturally occurring halogenated phenanthroindolizidine alkaloid. Compound (+)-1 displayed a selective in vitro cytotoxic effect against MDA-MB-468 cells (IC₅₀ 7.4 μM), while compound 2 showed pronounced in vitro cytotoxic activity against all three breast cancer cell lines tested (MDA-MB-468, MDA-MB-231, and MCF7; IC₅₀ values of 0.038-0.91 μM).
Amin OS. Malignant middle cerebral artery infarction. *BMJ Case Reports*, 2017; doi:10.1136/bcr-2016-219117. (CiteScore: 0.13; Tier: Q3).

**Malignant middle cerebral artery infarction**

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**Abstract**

A 55-year-old man with hypertension was referred from a rural hospital. Two days before, he had developed a cardioembolic ischaemic stroke, which resulted in left-sided hemiparesis and hemi-anaesthesia. On the day of referral, he developed repeated vomiting and severe headache, followed by progressive obtundation and coma. There was papilloedema. Both planter reflexes were extensors. A non-contrast CT brain scan was done (figure 1). The initial CT brain scan was not available for comparison. The patient was outside the international guidelines on timing of decompressive hemicraniectomy (DCH) for ischaemic stroke and was extremely unwell. After a few hours, he died from ‘malignant middle cerebral artery (MCA) infarction’.

**Abstract**

**Background:** A variety of ECG changes occur as an aftermath of stroke. Prolongation of the QTc interval is a well-documented change. We analyzed QTc interval prolongation among patients with acute hemorrhagic strokes.

**Methods:** This observational study was conducted at the Emergency Department of Sulaymaniyah General Teaching Hospital and Shar Hospital from September 1st, 2014 to August 31st, 2015. Fifty patients who developed acute spontaneous hypertensive intracerebral hemorrhage (ICH) and 50 patients who developed acute non-traumatic subarachnoid hemorrhage (SAH) were included in the study. All patients underwent resting 12-lead ECG within half an hour of admission. The QTc interval was calculated and analyzed in those 100 patients.

**Results:** Females (62%) outnumbered males (38%) with a female to male ratio of 1.6:1. Forty percent of the patients were between 60-69 years of age. Hypertension was seen in 82% of patients while left ventricular hypertrophy was documented in 40% of patients. The QTc was prolonged in 38 patients (17 patients in the ICH group and 21 patients in the SAH group). In both groups, males demonstrated QTc prolongation more than females. However, there were no statistically significant gender difference between both groups and within the same group. There was a statistically significant association between SAH and QTc prolongation (p-value<0.001); the ICH group did not demonstrate any significant relationship with QTc prolongation.

**Conclusion:** Prolongation in the QTc interval was “statistically” associated with acute SAH only. No gender difference was noted; whether this observation is clinically significant or not, it needs further analytic studies.

**Keywords:** subarachnoid hemorrhage, intracerebral hemorrhage, stroke, QTc interval prolongation, ECG.
Simultaneous left-sided hypertensive putaminal and thalamic haemorrhages

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Abstract
A woman aged 71 years with hypertension developed sudden severe headache and right-sided weakness. The blood pressure was 210/135 mm Hg. She was drowsy. Examination revealed right-sided upper motor neuron facial weakness, hemiparesis, hemi-anaesthesia and extensor planter reflex. Urgent non-contrast CT brain scan was done as shown in figures 1 and 2.
Abstract
An Iranian boy aged 15 years presented with a few day's history of abnormal gait and sudden repetitive jerky limbs' movements. The past histories were unremarkable. He was fully conscious. Examination revealed ataxia of stance and gait and generalised myoclonic jerks. Ocular examination revealed opsoclonus (video 1). Routine blood tests and brain MRI with gadolinium were normal. The boy's father stated that he intends to go back to Iran and manage his son there. In Iran, brain MRI, chest/abdomenopelvic CT scans, paraneoplastic autoantibodies panel and CSF analysis were unremarkable. The boy was diagnosed with idiopathic opsoclonus; partially improved on intravenous immunoglobulin.
Codfish vertebra sign

Osama S M Amin.

Department of Medicine, International Medical University School of Medicine, Negeri Sembilan, Malaysia.

Abstract
A woman aged 70 years presented with several years' history of low back pain and bilateral lower limb pains. Her menstrual cycles ceased when she was 44 years of age. Plain X-ray of the lumbosacral spine revealed diffuse osteoporotic changes (figure 1). A battery of investigations was performed; the only abnormal results were slightly raised serum alkaline phosphatase (probably from vertebral fractures) and very low-serum 25-hydroxyvitmain D. Lumbosacral spine MRI was ordered (figure 2) and revealed several codfish vertebrae in addition to lumber spinal stenosis. Dual X-ray absorptiometry revealed a T-score of −2.9 at the spine. The patient’s diagnosis was postmenopausal osteoporosis.
Feasibility of implementing chronic care model in the Malaysian public primary care setting

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Abstract

Introduction: Non-communicable diseases (NCD) is a global health threat. The Chronic Care Model (CCM) was proven effective in improving NCD management and outcomes in developed countries. Evidence from developing countries including Malaysia is limited and feasibility of CCM implementation has not been assessed. This study intends to assess the feasibility of public primary health care clinics (PHC) in providing care according to the CCM.

Methodology: A cross-sectional survey was conducted to assess the public PHC ability to implement the components of CCM. All public PHC with Family Medicine Specialist in Selangor and Kuala Lumpur were invited to participate. A site feasibility questionnaire was distributed to collect site investigator and clinic information as well as delivery of care for diabetes and hypertension.

Results: There were a total of 34 public PHC invited to participate with a response rate of 100%. There were 20 urban and 14 suburban clinics. The average number of patients seen per day ranged between 250-1000 patients. The clinic has a good mix of multidisciplinary team members. All clinics had a diabetic registry and 73.5% had a hypertensive registry. 23.5% had a dedicated diabetes and 26.5% had a dedicated hypertension clinic with most clinic implementing integrated care of acute and NCD cases.

Discussion: The implementation of the essential components of CCM is feasible in public PHCs, despite various constraints. Although variations in delivery of care exists, majority of the clinics have adequate staff that were willing to be trained and are committed to improving patient care.

Keywords: Chronic care model, chronic disease, non-communicable disease, feasibility, multifaceted intervention, Primary Healthcare clinic, Malaysia.
Anatomical knowledge among medical, dental and health science professionals

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⁴Semester 8, Chiropractic Program, International Medical University Malaysia.

Abstract
The discipline of anatomy is an integral part of curriculum for Medical, Dental and Health Sciences programs. The evolution in undergraduate medical school curricula has significantly impacted the anatomy education. The application of anatomical knowledge plays a crucial role in daily clinical practice. This review was aimed to evaluate the anatomical knowledge among the medical, dental and health science professionals, and their perceptions on application of anatomical knowledge in clinical practice. A computerized literature search which includes PubMed, Web of knowledge and Ovid Medline, was performed. The studies in the English language and published in year 2000 onwards were included. Most of the studies were done in UK and Spain followed by Australia, US and Canada. The studies conducted among Medical and Chiropractic professions were 50% and 14% respectively. The rest of the studies were done among dentistry, podiatry, physiotherapy, radiographer and nursing students. The students with preclinical exposure scored significantly higher than those without preclinical exposure. The medical students and clinical educators perceived that the application of anatomical knowledge is not strong enough for clinical practice. The virtual medical museum, case-based learning, peer-assisted learning, inter-professional forum and the recapitulation of anatomy in clinical years are suggested to improve in anatomy education. The curriculum design, early clinical exposure, revision of course content, adequacy of learning resources and assessment methods contribute to enhance the students’ learning and their ability to apply the anatomical knowledge in daily practice.

Keywords: Anatomical knowledge, application, Medical, Dental, Health Science Professionals.
Prevalence and clinical characteristics of metabolic syndrome among Malaysian hypertensive subjects using the international diabetes federation definition

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Abstract

Individuals with metabolic syndrome are at increased risk for developing cardiovascular disease and diabetes mellitus. This study was carried out to determine the prevalence of metabolic syndrome and clinical characteristics in hypertensive patients according to the criteria of the new International Diabetes Federation (IDF) definition. Hypertensive patients were recruited from the Medical Out-Patient Department, Kuantan Hospital. The five components of metabolic syndrome were examined which included blood pressure (≥130/85 mmHg), fasting glucose (≥5.6mmol/L), fasting triglycerides (≥1.7 mmol/L), high-density lipoprotein (HDL) cholesterol level (<1.03mmol/L in males and <1.29mmol/L in females), and abdominal obesity (waist circumference: men>90cm; women>80cm). Out of 139 hypertensive patients, there were 113 met all the selection criteria consisted of 61 male and 52 female subjects. The participants’ age ranged from 21 to 91 years (51.9±16.8 years; mean±SD), and body mass index 13.5-42.3 kg/m\textsuperscript{2} (27.5±4.9 kg/m\textsuperscript{2}). According to the IDF criteria, the prevalence of central obesity was 67.2\% in men and 84.6\% in women. Among the 113 hypertensive subjects over 21 years of age, 51 subjects or 45.1\% had metabolic syndrome. The present data revealed that there was high prevalence of metabolic syndrome in Malaysian hypertensive subjects. This finding was supported by the fact of high prevalence of central obesity among the study subjects.

Keywords: clinical characteristics, prevalence, metabolic syndrome, hypertension.

Tomorrow’s doctors and dentists in Malaysia: Empathic or indifferent?

Muneer Gohar Gohar Babar, Syed Shahzad Hasan, Lee Ping Lim, Phei June Lim, Nik Mohd Mazuan Nik Mohd Rosdy, Siti Fauzza Binti Ahmad.

Abstract

Objectives: This study compared the empathic behaviour of first year to final year dental and medical students in Malaysia and explored whether academic training of dental and medical students increases their subjective empathic tendencies.

Methods: This cross-sectional study was carried out among 1020 first year to final year (fifth-year) undergraduate medical and dental students using a validated, self-administered Jefferson Scale of Empathy-Health Care Provider Student Version (JSE-HPS) questionnaire. The data were collected from first year to final year (fifth-year) students enrolled in Bachelor of Medicine/Bachelor of Surgery (MBBS) and Bachelor of Dental Surgery (BDS) degree programs at 2 government-funded universities and one private university.

Results: Dental students had a significantly higher total mean empathy score than medical students (84.11 versus 81.96, p < 0.05). However, medical students had a narrow actual score range (59.35 - 133.35) than dental (22.05 - 133.35) students. Males (Medical: 82.57, Dental: 84.97) and students of Malay origin (Medical: 82.52, Dental: 85.11) were more empathic than females and students of other ethnic origins. The results also indicate that third-year medical students (mean: 82.95) and fourth-year dental students (mean: 86.36) were more empathic than students in other professional years.

Conclusions: We recommend the use of some form of active training and assessment to assist in the development of empathy in medical and dental students. Medical and dental schools should place more emphasis on teaching empathic communication.

Keywords: Dental-students, medical-students, empathy, indifferent, JSE-HPS, Malaysia.
Babar MG, Hasan SS, Yong WM, Mitha S, Al-Waeli HA. Patients' perceptions of dental students' empathic, person-centered care in a dental school clinic in Malaysia. *Journal of Dental Education*, 2017; 81(4): 404-412. (ISI IF: 0.972; CiteScore: 0.77; Tier: Q3).

**Patients' perceptions of dental students' empathic, person-centered care in a dental school clinic in Malaysia**

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²All the authors contributed equally to this study. Dr. Babar is Associate Professor and Program Director, School of Dentistry, International Medical University, Kuala Lumpur, Malaysia; Dr. Hasan is Lecturer, School of Pharmacy, International Medical University, Kuala Lumpur, Malaysia; Wong Mei Yong was a student pursuing a BPharm degree, International Medical University, Kuala Lumpur, Malaysia at the time of the study; Dr. Mitha is Senior Lecturer, School of Dentistry, International Medical University, Kuala Lumpur, Malaysia; and Dr. Al-Waeli is pursuing a PhD at Faculty of Dentistry, McGill University, Canada.

**Abstract**

Empathy has been identified as a crucial foundation in building an effective dentist-patient relationship. The aim of this study was to assess patients' perceptions of dental students' empathic care in the primary oral health care clinic at International Medical University in Kuala Lumpur, Malaysia in May-October 2014. The study also assessed the validity and reliability of the Consultation and Relational Empathy (CARE) Measure in this setting; the association between number of encounters and students' CARE Measure scores; and the association between students' empathy (measured by the Toronto Empathy Questionnaire) and CARE Measure scores. Participants were 283 patients (aged ≥18 years) who were asked to self-complete the ten-item CARE Measure immediately after their clinical encounter with students who provided care under supervision of the teaching staff. The results showed that the CARE Measure demonstrated good internal consistency (Cronbach’s α=0.95). A single factor solution emerged, accounting for 69% of the variance. The mean CARE Measure score in the consultations was 43.55±6.14, and 26% of the students achieved the maximum possible score of 50. The mean number of encounters with each student was 2.33±2.78. An increase of one episode was associated with an insignificant average CARE score decrease of 0.05 (-0.28, 0.38), whereas students' empathy was associated with a small increase in average CARE Measure score of 0.63 (0.08, 1.18). These results provide evidence of the measure’s ability to support feedback to dental students on their empathy when interacting with patients.

**Keywords:** CARE Measure, clinical education, dental education, dentist-patient relations, empathy.

**Student preparedness characteristics important for clinical learning: Perspectives of supervisors from medicine, pharmacy and nursing**

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⁵School of Medicine, Perdana University, Selangor, Malaysia;
⁶School of Pharmacy, Monash University, Selangor, Malaysia;
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**Abstract**

**Background:** Student perspectives of clinical preparedness have been studied in the literature, but the viewpoint of supervisors is limited. Hence, the aim was to examine the perspective of supervisors on the characteristics of health professional students important for preparedness for clinical learning.

**Methods:** This was a descriptive, questionnaire-based, cross-sectional study conducted at three higher education institutions in Malaysia. A previously published questionnaire with 62 characteristics was adopted with modifications after pre-testing. Descriptive analysis was completed for the demographic data. The sample was grouped based on health profession, clinical practice experience and teaching experience for further analysis. Non-parametric Kruskal-Wallis test was selected to evaluate differences in mean ranks to assess the null hypothesis that the medians are equal across the groups. Kruskal-Wallis post-hoc pair wise comparison was performed on samples with significant differences across samples.

**Results:** The sample was comprised of 173 supervisors from medicine (55, 32%), pharmacy (84, 48%) and nursing (34, 20%). The majority (63%) of the supervisors were currently in professional practice. A high percentage (40%) of supervisors had less than 4 years of teaching experience. The highest theme ratings were for willingness (6.00) and professionalism (5.90). There was a significant difference (p < 0.05) in the medians, among medicine, pharmacy and nursing professional speciality for willingness (5.70, 6.00 and 6.00), professionalism (5.70, 5.90 and 6.15), communication and interaction (5.42, 5.67 and 6.00), personal attributes (5.42, 5.71 and 6.02) and the professional and interpersonal skills (5.50, 5.63 and 6.00) themes. Post-hoc analysis showed a significant difference (p < 0.05) between medicine and nursing groups in the willingness (5.70 and 6.00), professionalism (5.70 and 6.15) and personal attributes (5.42 and 6.02) themes. Supervisors who are currently in practice had given high ratings compared to other groups. There were no significant differences observed within groups with different level of teaching experiences.
Conclusions: All supervisors rated professionalism and willingness as the most important characteristics followed by personal attributes. Further strengthening learning opportunities related to these characteristics in the curriculum may improve the students' preparedness in clinical learning.

Keywords: Clinical preparedness, Supervisor’s perspective, Clinical learning.
Effect of elevated temperature on the physiological responses of marine *Chlorella* strains from different latitudes

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Abstract

The increased frequency of heat waves due to climate change poses a threat to all organisms. Microalgae are the basis of aquatic food webs, and high temperatures have significant impacts on their adaptation and survival rates. Algae respond to environmental changes by modulating their photosynthetic rates and biochemical composition. This study aims to examine the effect of elevated temperature on similar taxa of marine *Chlorella* originating from different latitudes. Strains from the Antarctic, temperate zone, and the tropics were grown at various temperatures, ranging from 4 to 38, 18 to 38, and 28 to 40 °C, respectively. A pulse-amplitude modulated (PAM) fluorometer was used to assess their photosynthetic responses. Parameters including maximum quantum efficiency (F\(_{V}/F_{M}\)), relative electron transport rate (rETR), and light harvesting efficiency (\(\alpha\)) were determined from the rapid light curves (RLCs). In addition, the composition of fatty acids was compared to evaluate changes induced by the temperature treatments. Increasing the temperature from 35 to 38 °C for both Antarctic and temperate strains and from 38 to 40 °C for the tropical strain resulted in severe inhibition of photosynthesis and suppressed growth. Although all the strains demonstrated the ability to recover from different stress levels, the tropical strain was able to recover most rapidly while the Antarctic strain had the slowest recovery. The results underline that the thermal threshold for the analysed *Chlorella* strains temperature ranges between 38 and 40 °C. Furthermore, the analysed strains exhibited different trends in their response to elevated temperatures and recovery capabilities.

Keywords: Global warming, Heat stress, Photosynthesis, F\(_{V}/F_{M}\).

**Evaluation of the predictive performance of bleeding risk scores in patients with non-valvular atrial fibrillation on oral anticoagulants**

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**Abstract**

**What is Known and Objective:** Bleeding risk scores (BRSs) aid in the assessment of oral anticoagulant-related bleeding risk in patients with atrial fibrillation. Ideally, the applicability of a BRS needs to be assessed, prior to its routine use in a population other than the original derivation cohort. Therefore, we evaluated the performance of 6 established BRSs to predict major or clinically relevant bleeding (CRB) events associated with the use of oral anticoagulant (OAC) among Malaysian patients.

**Methods:** The pharmacy supply database and the medical records of patients with non-valvular atrial fibrillation (NVAF) receiving warfarin, dabigatran or rivaroxaban at two tertiary hospitals were reviewed. Patients who experienced an OAC-associated major or CRB event within 12 months of follow-up, or who have received OAC therapy for at least 1 year, were identified. The BRSs were fitted separately into patient data. The discrimination and the calibration of these BRSs as well as the factors associated with bleeding events were then assessed.

**Results:** A total of 1017 patients with at least 1-year follow-up period, or those who developed a bleeding event within 1 year of OAC use, were recruited. Of which, 23 patients experienced a first major bleeding event, whereas 76 patients, a first CRB event. Multivariate logistic regression results show that age of 75 or older, prior bleeding and male gender are associated with major bleeding events. On the other hand, prior gastrointestinal bleeding, a haematocrit value of less than 30% and renal impairment are independent predictors of CRB events. All the BRSs show a satisfactory calibration for major and CRB events. Among these BRSs, only HEMORR²HAGES (C-statistic = 0.71, 95% CI 0.60-0.82, P < .001) and ATRIA score (C-statistic = 0.70, 95% CI 0.58-0.82, P < .001) show acceptable discrimination performance for major bleeding events. All the 6 BRSs, however, lack acceptable predictive performance for CRB events.

**What is New and Conclusion:** To the best of our knowledge, this is the first evaluation study of the predictive performance of these 6 BRSs on clinically relevant bleeding events applied to the same cohort consisting of mainly Asian novel oral anticoagulant users. These BRSs show poor to acceptable predictive performance on OAC-induced major or CRB events. An improvement in the existing BRSs for OAC users is warranted.

**KEYWORDS:** adverse effects, dabigatran, haemorrhage, oral anticoagulants, predictive performance, risk assessment, risk scores, rivaroxaban, stroke prevention, warfarin.
Assessment of the predicted rate and associated factors of dabigatran-induced bleeding events in Malaysian patients with non-valvular atrial fibrillation

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Abstract

Purpose: To assess the predicted rate and the factors associated with bleeding events among patients with non-valvular atrial fibrillation (NVAF) receiving dabigatran therapy.

Methods: This retrospective cohort study includes adult patients of two tertiary hospitals in Malaysia. Potential study subjects were identified using pharmacy supply database or novel oral anticoagulant (NOAC) registry. Demographics, clinical data and laboratory test results were extracted from the medical records of the patients or electronic databases. The main outcome measure is the occurrence of a bleeding event. Bleeding events were classified into major bleeding, clinically relevant non-major bleeding, or minor bleeding, according to the International Society on Thrombosis and Haemostasis criteria. We consider clinically relevant non-major bleeding events or major bleeding events as clinically relevant bleeding events. An occurrence of any bleeding event was recorded from the initiation of NOAC therapy until the death of a patient, or the date of permanent discontinuation of NOAC use, or the last day of data collection. The predicted rate of dabigatran-induced bleeding events per 100 patient years was estimated.

Results: During a median follow-up period of 18 months, 73 patients experienced 90 bleeding events. Among these patients, 25 including 4 fatal cases, experienced major bleeding events. The predicted rate per 100 patient-years of follow-up of any bleeding events was 9.0 [95% CI 6.9 to 11.1]; clinically relevant bleeding events 6.0 [95% CI 4.8 to 8.3], and major bleeding events 3.0 [95% CI 1.9 to 4.2]. The independent risk factor for clinically relevant bleeding events is prior bleeding. While prior bleeding or congestive heart failure is linked with major bleeding events.

Conclusions: The predicted rate for dabigatran-induced major bleeding episodes is low but these adverse events carry a high fatality risk. Preventive measures should target older patients who have prior bleeding or congestive heart failure.
Moxifloxacin loaded chitosan gel formulations for the treatment of periodontal diseases

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Abstract
For treatment of periodontal diseases, the local delivery of antimicrobials into periodontal pocket has been shown to be more effective than the systemic delivery. However, the major challenge for the formulators is the removal of the delivery system from the application side due to the salivation as well as the movement of the tongue. Mucoadhesive polymers have been successfully utilized to go over this obstacle. In recent years, particularly chitosan has been widely investigated for periodontal delivery systems not only for its mucoadhesive properties but also for its antimicrobial activity. In our study, we developed a local delivery system for an antimicrobial drug, moxifloxacin hydrochloride (MF), at 0.5% w/v, using chitosan for the treatment of periodontal diseases. For comparison, formulations based on two other mucoadhesive polymers, carbomer (Carbopol 940®) and hydroxypropyl methylcellulose(HPMC) were also prepared. Viscosity, mucoadhesion, drug release and permeation properties as well as the antimicrobial activity of the gel formulations was evaluated in vitro. The developed formulations with a suitable viscosity for application were found to remain on the mucosa and release the drug in a prolonged fashion. Drug release from the formulations was found to be dependent on the viscosity of the formulations. A relative correlation was found between viscosity and mucoadhesion for the polymers investigated, with an order of HPMC>Carbopol®=Chitosan. Permeation of the drug was increased in presence of chitosan. The antimicrobial activity of MF against Staphylococcus aureus and Streptococcus mutans were found to be enhanced with the developed formulations. The highest antimicrobial activity was observed with the chitosan-based formulations, due to the synergic effect of chitosan itself. Our results showed that chitosan based formulation is a promising local delivery system for treatment of periodontal disease by increasing the effect of the drug due to its mucoadhesive and penetration enhancing effect as well its antimicrobial activity. Furthermore, with these properties the developed formulations will provide reduced frequency of administration, which result in higher patient compliance.
Effect of maleic anhydride-modified poly(lactic acid) on the properties of its hybrid fiber biocomposites

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Abstract
This work investigated the effect of maleic anhydride (MA)-modified poly(lactic acid) (PLA), which is melt-blended with different untreated and aqueous borax (BR)-treated hybrid oil palm empty fruit bunch fibers (EFBF)/Kenaf core fibers (KCF), and compression-molded into corresponding hybrid biocomposites. These hybrid systems include BR-treated EFBF/BR-treated KCF reinforced MA-modified PLA i.e., BR(EFBF-KCF)-MAPLA, BR-treated EFBF/BR-treated KCF reinforced unmodified PLA i.e., BR(EFBF-KCF)-PLA, untreated EFBF/untreated KCF reinforced MA-modified PLA i.e., EFBF(KCF)-MAPLA, and untreated EFBF/untreated KCF reinforced unmodified PLA i.e., EFBF-KCF-PLA respectively. Characterizations of the hybrid systems revealed that optimal mechanical, physical, morphological, thermal and dynamic mechanical properties were provided by the BR(EFBF-KCF)-MAPLA, resulting from improved interface adhesion, consequent of the synergistic influence of BR treatment of natural fibers, and the compatibilization effect provided by the MA-modified PLA. The grafting degree and efficiency of MA onto the PLA backbone was appreciable, as indicated by direct titration, and through monitoring using Fourier Transform Infrared Spectroscopy (FTIR); thus the MA-modified PLA facilitated the formation of strong interface adhesion with the BR-treated hybrid fibers. The BR(EFBF-KCF)-MAPLA showed promising properties for usage as a bio-inspired, and sustainable alternative fiberboard article.

Keywords: poly(lactic acid), maleic anhydride, hybrid biocomposites, bio-inspired.
Dermatofibrosarcoma protuberance of the breast: A diagnostic challenge

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Abstract

Dermatofibrosarcoma protuberans (DFSP) is an uncommon slow growing neoplasm of the dermis with tendency to invade the subcutaneous tissues. It presents during the third to fourth decade of life and is commonly seen over the trunk, extremities and head and neck. DFSP presenting as a breast lump is rare but few cases have been reported in the literature. Preoperative diagnosis with mammography, ultrasonography and FNAC is challenging. We report a case of a DFSP of the right breast in a middle aged lady with history of recurrent breast lumps excised and diagnosed in the past as benign. She presented with progressively increasing right breast lump of 2 months duration. She underwent wide local excision and histology revealed dermatofibrosarcoma protuberans. In view of its local aggressiveness with incomplete surgical margin, mastectomy was performed.

Keywords: Breast, Dermatofibrosarcoma protuberans, Immunohistochemical stains, Mastectomy.
Renal target potentials of a polymeric drug carrier, poly-L-glutamic acid, in normal and diabetic rats

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Abstract

Background and purpose: Poly-L-glutamic acid (PG) has been used widely as a carrier to deliver anticancer chemotherapeutics. This study evaluates PG as a selective renal drug carrier.

Experimental approach: 3H-deoxycytidine-labeled PGs (17 or 41 kDa) and 3H-deoxycytidine were administered intravenously to normal rats and streptozotocin-induced diabetic rats. The biodistribution of these compounds was determined over 24 h. Accumulation of PG in normal kidneys was also tracked using 5-(aminoacetamido) fluorescein (fluoresceinyl glycine amide)-labeled PG (PG-AF). To evaluate the potential of PGs in ferrying renal protective anti-oxidative stress compounds, the model drug 4-(2-aminoethyl)benzenesulfonyl fluoride hydrochloride (AEBSF) was conjugated to 41 kDa PG to form PG-AEBSF. PG-AEBSF was then characterized and evaluated for intracellular anti-oxidative stress efficacy (relative to free AEBSF).

Results: In the normal rat kidneys, 17 kDa radiolabeled PG (PG-Tr) presents a 7-fold higher, while 41 kDa PG-Tr shows a 15-fold higher renal accumulation than the free radiolabel after 24 h post injection. The accumulation of PG-AF was primarily found in the renal tubular tissues at 2 and 6 h after an intravenous administration. In the diabetic (oxidative stress-induced) kidneys, 41 kDa PG-Tr showed the greatest renal accumulation of 8-fold higher than the free compound 24 h post dose. Meanwhile, the synthesized PG-AEBSF was found to inhibit intracellular nicotinamide adenine dinucleotide phosphate oxidase (a reactive oxygen species generator) at an efficiency that is comparable to that of free AEBSF. This indicates the preservation of the anti-oxidative stress properties of AEBSF in the conjugated state. Conclusion/Implications: The favorable accumulation property of 41 kDa PG in normal and oxidative stress-induced kidneys, along with its capabilities in conserving the pharmacological properties of the conjugated renal protective drugs, supports its role as a potential renal targeting drug carrier.

Keywords: carboxylated polymers, carboxylated polypeptides, carrier, diabetes, renal drug delivery, acute kidney injury, chronic renal failure, end-stage renal failure.
Forensic age estimation of Chinese Malaysian adults by evaluating occlusal tooth wear using modified Kim’s index

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Abstract
Background and Objective: Evaluation of dental attrition is an easy and relatively accurate approach to estimating the age of an adult either ante- or postmortem for some specific population. Dental attrition represents a progressive physiological age change that can be measured using variety of indices to aid as an adjunct in forensic age estimation. Some of the previously proposed indices have their own practical limitations. This paper focuses on using modified Kim’s criteria to score dental attrition to estimate the age of Chinese Malaysian adults and validate it.

Methodology: Tooth wear was evaluated on 190 dental models of Chinese Malaysian adults (age range: 20–60 years) using modified Kim’s index to custom-derive a population specific linear equation. The same equation was validated further on new 60 dental casts.

Results and Conclusion: Regression analysis revealed good correlation between age and teeth wear and lower standard error of estimate. Test of regression on a test sample (n = 30 pairs, age range: 20–60 years) showed insignificant difference between predicted versus the actual age with statistically acceptable mean absolute difference. These data suggest that modified Kim’s index can be used effectively in forensic age estimation.

**Treatment of radiation-induced erectile dysfunction with low-intensity extracorporeal shock wave: A case report**

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**Abstract**

Low-intensity extracorporeal shock wave therapy is a new treatment in treating vasculogenic erectile dysfunction. We report a case of low-intensity extracorporeal shock wave therapy used for treating radiation-induced erectile dysfunction. A 66-year-old gentleman with dyslipidemia and smoking presented with radiation-induced erectile dysfunction. Six sessions of low-intensity extracorporeal shock wave therapy were administered. Pre-treatment IIEF-5 score was 10 and post-treatment IIEF-5 score at one month was 19. Low-intensity extracorporeal shock wave therapy has the potential to treat radiation-induced erectile dysfunction.

**Keywords:** Erectile dysfunction, prostate cancer, radiation therapy, shock wave.
Synergistic effect of nonsteroidal anti-inflammatory drugs (NSAIDs) on antibacterial activity of cefuroxime and chloramphenicol against methicillin-resistant Staphylococcus aureus

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Abstract
Objectives: Currently, only a few antibiotics are available to treat methicillin-resistant Staphylococcus aureus (MRSA). One alternative approach includes adjuvants to antibiotic therapy. Non-steroidal anti-inflammatory drugs (NSAIDs) are non-antibiotic drugs reported to exhibit antibacterial activity. The objective of this study was to investigate the interaction between NSAIDs with selected antibiotics (cefuroxime and chloramphenicol) against strains of S. aureus.

Methods: The antibacterial activity of four NSAIDs (aspirin, ibuprofen, diclofenac and mefenamic acid) were tested against ten pathogenic bacterial strains using the microdilution broth method. The interaction between NSAIDs and antibiotics (cefuroxime/chloramphenicol) was estimated by calculating the fractional inhibitory concentration (FICI) of the combination.

Results: Aspirin, ibuprofen and diclofenac exhibited antibacterial activity against the selected pathogenic bacteria. The interaction between ibuprofen/aspirin with cefuroxime was demonstrated to be synergistic against methicillin-sensitive S. aureus (MSSA) and the MRSA reference strain, whereas for MRSA clinical strains additive effects were observed for both NSAIDs and cefuroxime combinations. The combination of chloramphenicol with ibuprofen/aspirin was synergistic against all of the tested MRSA strains and displayed an additive effect against MSSA. A 4–8192-fold reduction in the cefuroxime minimum inhibitory concentration (MIC) and a 4–64-fold reduction of the chloramphenicol MIC were documented.

Conclusions: Overall, the NSAIDs ibuprofen and aspirin showed antibacterial activity against strains of S. aureus. Although individually less potent than common antibiotics, these NSAIDs are synergistic in action with cefuroxime and chloramphenicol and could potentially be used as adjuvants in combating multidrug-resistant MRSA.

Keywords: Cefuroxime, Chloramphenicol, NSAIDs, Non-steroidal anti-inflammatory drugs, Staphylococcus aureus, Synergy.
Chang SK, Ismail A, Yanagita T. Characterization of antioxidative peptides from the oil palm (Elaeis guineensis Jacq.) kernel protein hydrolysate. *Annals of Nutrition and Metabolism*, 2017; 71(Suppl.2): 1172. (ISI IF: 2.424; CiteScore: 2.69; Tier: Q2).

**Characterization of antioxidative peptides from the oil palm (Elaeis guineensis Jacq.) kernel protein hydrolysate**

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**Abstract**

**Background and objectives:** Plant proteins play essential roles in human nutrition. Oil palm fruit is the most important oilseed crops globally where its kernel is obtained as waste after palm oil production. Our previous study demonstrated that oil palm kernel protein hydrolysate (OPKH) obtained after pepsin-pancreatin hydrolysis showed strong antioxidant activity. Hence, this study aims to purify and identify the antioxidative peptides from OPKH.

**Methods:** First, the OPKH was purified by ultrafiltration, followed by reversed-phase (analytical) and semi-preparative HPLC to collect the bioactive fractions. Subsequently, antioxidant capacities (ACs) of the purified peptides from OPKH were evaluated using ferric reducing antioxidant power (FRAP), β-carotene-linoleate bleaching (BCB) assay and 2,2′-azino-bis(3-ethylbenzthiazoline-6-sulphonic acid) (ABTS) radical scavenging activity assay. In relation, the amino acid compositions of the purified peptide fractions were also determined. Finally, the amino acid sequence of the antioxidative peptide was identified by electrospray ionization/multi-stage mass spectrometry (ESI/MS/MS) coupled with Q-TOF LC/MS and PEAKS studio software using de novo sequencing.

**Results:** Nine active fractions (F1-F9) were collected and purified. Fraction F6 showed the highest AC. Fraction F6 was collected and re-chromatographed on the same analytical column where three sub-fractions (F6a, F6b and F6c) were obtained. Three antioxidative peptides, Val-Val-Gly-Asp-Gly-Asp-Val (VVGGDGDV), Val-Pro-Val-Thr-Ser-Thr (VPVTST) and Leu-Thr-Thr-Leu-Asp-Ser-Glu (LTTLDSE) in this fraction F6 were identified using MS/MS. The molecular masses of the peptides VVGGDGDV, VPVTST and LTTLDSE were 717.34, 602.3 and 777.37 Da, respectively. The three peptides did not show any similarity with other antioxidant peptides listed in BLAST database of NCBI.

**Conclusions:** Three novel peptides with ACs from OPKH were characterized. These active peptides may be useful as ingredients for food products and nutraceutical applicants.

**Keywords:** oil palm kernel protein hydrolysate (OPKH), antioxidant capacity (AC), peptide, amino acid sequence, LC-MS/MS.
Chang SMW, Wai SX, Chin PY, Lim JT, Mitra NK. Evaluation of changes in the locomotion and histology of sciatic nerve following experimental autoimmune encephalomyelitis. *Journal of Morphological Sciences, 2017; 34(4): 241-246. (CiteScore: 0.16; Tier: Q4).*

**Evaluation of changes in the locomotion and histology of sciatic nerve following experimental autoimmune encephalomyelitis**

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**Abstract**

**Introduction:** Involvement of peripheral nerves in the experimental model of multiple sclerosis (MS) is rarely observed. The objective of this study was to investigate the changes in the locomotion in a mouse model of experimental autoimmune encephalomyelitis (EAE) and correlate with histological changes, if any, in the sections of sciatic nerve and lumbar part of spinal cord.

**Material and Methods:** C57BL/6 mice (10 weeks, n = 8) were immunized with single subcutaneous injection of 300 μg of MOG35-55 and 200 μL of complete Freund’s adjuvant (CFA) to produce EAE models. Limp tail with weakness of hindlimb was observed on day 10 and improvement in the weakness was observed on day 20 onwards. Footprint analysis was done to evaluate the impairment in the locomotion on day 0, 5, 10, 15 and 20 of the experiment.

**Results:** One way repeated measure ANOVA found significant reduction in the mean hindlimb stride length on day 10 and 15 (left) and on day 15 and day 20 (right) when compared to mean stride length in day 0 (p<0.05). Histological analysis showed evidence of macrophage infiltration around the dilated blood vessels in the epineurium of sciatic nerve and evidence of damage in the myelinated white matter of lateral funiculus of the lumbar sections of the spinal cord in EAE mice.

**Conclusion:** It is concluded that in mouse model of EAE, the impairment of locomotion due to damage in the lumbar part of spinal cord can be associated with inflammatory changes in the sciatic nerve.

**Keywords:** experimental autoimmune encephalomyelitis, footprint analysis, histology, sciatic nerve, spinal cord.
Squamous-cell carcinoma of the mouth

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Abstract

A 54-year-old woman presented to a dental clinic with a 1-year history of oral swelling and a sore mouth. She had regularly chewed loose-leaf tobacco, which she had placed on the floor of her mouth between the jaw and tongue, up to five times each day for more than 10 years. Intraoral examination revealed an irregular, indurated lesion that measured 3 cm in its greatest dimension and was located on the floor of the mouth inside the left jaw (Panel A). Incisional biopsy of the lesion revealed invasive squamous-cell carcinoma with hyperchromic, pleomorphic cells and a “keratin pearl” (Panel B, arrow) in the connective tissue. Computed tomography and positron-emission tomography showed no bony or lymph-node involvement. Squamous-cell carcinoma is the most common type of neoplasm of the oral cavity. The patient underwent an en bloc excision of the carcinoma as well as segmental mandibulectomy with the use of a vascularized free fibular flap as an osteocutaneous graft and selective neck dissection. Pathological analysis revealed no involvement of bone or lymph nodes, with tumor-free margins. The patient was advised to stop using tobacco products. Two years after treatment, she remained free of recurrence.

The role of pazopanib on tumour angiogenesis and in the management of cancers: A review

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Abstract

Pazopanib is a relatively new compound to be introduced into the chemotherapy field. It is thought to have decent anti-angiogenic properties, which gives an additional hope for the treatment of certain types of cancers. A systematic review solely discussing about pazopanib and its anti-angiogenic effect is yet to be published to date, despite several relevant clinical trials being conducted over the recent years. In this review, we aim to investigate the mechanism of pazopanib's anti-angiogenic effect and its effectiveness in treating several cancers. We have included, in this study, findings from electronically searchable data from randomized clinical trials, clinical studies, cohort studies and other relevant articles. A total of 352 studies were included in this review. From the studies, the effect of pazopanib in various cancers or models was observed and recorded. Study quality is indefinite, with a few decent quality articles. The most elaborately studied cancers include renal cell carcinoma, solid tumors, advanced solid tumors, soft tissue sarcoma, breast cancer and gynecological cancers. In addition, several less commonly studied cancers are included in the studies as well. Pazopanib had demonstrated its anti-angiogenic effect based on favorable results observed in cancers, which are caused by angiogenesis-related mechanisms, such as renal cell carcinoma, solid tumors, advanced solid tumors and soft tissue sarcoma. This review was conducted to study, analyze and review the anti-angiogenic properties of pazopanib in various cancers. The results obtained can provide a decent reference when considering treatment options for angiogenesis-related malignancies. Furthermore, the definite observations of the anti-angiogenic effects of pazopanib could provide newer insights leading to the future development of drugs of the same mechanism with increased efficiency and reduced adverse effects.

Keywords: Angiogenesis, Blood vessels, Cancer, Pazopanib, Systemic review, Vascular endothelial growth factor.

**Vesicular systems containing curcumin and their applications in respiratory disorders - A mini review**

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**Abstract**

**Background:** Vesicular systems like nanotechnology and liposomes are gaining tremendous attention lately in the field of respiratory diseases. These formulations enhance bioavailability of the drug candidate, which could be achieved through a novel drug delivery mechanism. Moreover, the therapeutic potential achieved through these systems are highly controllable over long durations of time providing better efficacy and patient compliance.

**Methods:** We have collated and summarized various recent attempts made to develop different controlled release drug delivery systems containing curcumin which would be of great interest for herbal, formulation and biological scientists.

**Results:** Different vesicular systems containing curcumin, are being studied for its therapeutic potential in different respiratory diseases. There has been a renewed interest in formulations containing curcumin recently, primarily owing to the broad spectrum therapeutic potential of this miracle substance. Various types of formulations, containing curcumin, targeting different bodily systems have recently emerged and, nevertheless, the search for newer frontiers with this drug goes on.

**Conclusions:** This mini review, in this direction, tries to highlight the key research interventions employing vesicular systems of drug delivery with curcumin.

**Keywords:** Nanotechnology, curcumin, liposomes.

Nanotechnology and diabetic wound healing - A review

Dinesh Kumar Chellappan, Yap Yenese, Chew Chian Wei, Gaurav Gupta.

Abstract
The incidence of diabetes has been on the rise and the rate of rise since the turn of this century has been phenomenal. One of the various battling issues faced by diabetics all over the globe is the management of diabetic wounds. Currently there are several management strategies to deal with the treatment of diabetic wounds. The conventional methods have several limitations. One of the major limitations is the rate and progression of healing of a diabetic wound when adopting a conventional diabetic wound management therapy. Lately, several nano techniques and nano products have emerged in the market that offer promising results for such patients. The treatment outcomes are achieved more efficiently with such nanomedical products. This review attempts to look into the currently available nanotechnological applications in the management of diabetic wounds. We take a deeper look into the available nanotherapeutic agents and the different nanocarriers that could be used in the management of diabetic wound healing. Lately, researchers around the globe have started providing evidences on the effective use of such nanoparticles in various fields of Medicine extending from genetics to various other branches of medicine. This also includes the management of diabetic wounds. This paper also discusses the challenges faced with these nanotherapies and nanoparticles with regard to the treatment of diabetic wounds.

Keywords: Nanotechnology, diabetes, diabetic wound healing, nanotherapeutic agents, nanocarriers.

An overview of pharmacological activities of Syzygium sp

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Division of Applied Biomedical Science and Biotechnology, School of Health Sciences, International Medical University, Kuala Lumpur, Malaysia

Abstract

Syzygium sp. is categorized under the Myrtaceae family. The plants are commonly found in Africa, Madagascar, Southeast Asia, Australia and other regions. There are more than 1000 species that are recorded under the Syzygium genus of which S. aromaticum, S. cumini and S. jambos are among the few famous for their medicinal properties. S. aromaticum is well known for its antibacterial, antifungal and antioxidant properties while S. cumini is known to treat diarrhea, digestive problems, cough and diabetes. S. cumini is also reported to have antioxidant and antimicrobial properties. On the other hand, S. jambo has been reported for its antioxidant, antibacterial and anti-inflammatory properties. Considering the vast health benefits brought by Syzygium species, this review discusses the various pharmacological activities of different Syzygium species, including anti-diabetic, antioxidant, antibacterial, antifungal, anticancer, anti-diarrheal, anti-amnesic and anti-inflammatory effects.

Keywords: Syzygium sp, Anti-diabetic, Antioxidant, Antibacterial, Antifungal, Anticancer, Anti-diarrheal, Anti-amnesic, Anti-inflammatory.
Chieng BW, Ibrahim NA, Then YY, Loo YY. Epoxidized jatropha oil as a sustainable plasticizer to poly(lactic acid). *Polymers*, 2017; 9: 204. (ISI IF: 3.364; CiteScore: 3.74; Tier: Q1).

**Epoxidized jatropha oil as a sustainable plasticizer to poly(lactic acid)**

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**Abstract**

A renewable resource, epoxidized jatropha oil (EJO), was used as a green plasticizer and added to poly(lactic acid) (PLA). EJO was compounded into PLA at different contents. The addition of 3 wt % EJO to the PLA demonstrates significant improvement in flexibility, which leads to a percentage increase of about 7000% in elongation at break. This tensile result was confirmed by surface morphology analysis with clear proof of plastic deformation in EJO-plasticized PLA. EJO imparts a good heat stabilization effect. Thermal stability of PLA was enhanced upon addition of EJO, which is due to their good interaction and plasticizer dispersion within the PLA matrix. This EJO-plasticized PLA has wide applications in various industries, such as packaging of food and non-food products.

**Keywords:** jatropha oil, epoxidized oil, plasticizer, poly(lactic acid).

**Isolation and characterization of cellulose nanocrystals from oil palm mesocarp fiber**

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**Abstract**

The aim was to explore the utilization of oil palm mesocarp fiber (OPMF) as a source for the production of cellulose nanocrystals (CNC). OPMF was first treated with alkali and then bleached before the production of CNC by acid hydrolysis (H₂SO₄). The produced materials were characterized using Fourier transform infrared (FTIR) spectroscopy, X-ray diffraction (XRD), thermogravimetric analysis (TGA), a scanning electron microscope (SEM) and a transmission electron microscope (TEM). It was proven that acid hydrolysis can increase the crystallinity of bleached OPMF and reduce the dimension of cellulose to nano scale. Changes in the peaks of the FTIR spectrum at 2852 (C-H stretching), 1732 (C=O stretching) and 1234 cm⁻¹ (C-O stretching) indicated that the alkali treatment completely removed hemicelluloses and lignin from the fiber surface. This can be seen from the thermogram obtained from the TGA characterization. Morphological characterization clearly showed the formation of rod-shaped CNCs. The promising results prove that OPMF is a valuable source for the production of CNC.

**Keywords:** mesocarp fiber, oil palm, cellulose.

**Generation of a MLL-AF9-specific stem cell model of acute monocytic leukemia**

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**Abstract**

Acute monocytic leukemia (AML-M5), a subtype of acute myeloid leukemia (AML), affects mostly young children and has poor prognosis. The mechanisms of treatment failure of AML-M5 are still unclear. In this study, we generated iPSC from THP-1 cells from a patient with AML-M5, using retroviruses encoding the pluripotency-associated genes (OCT3/4, SOX2, KLF4 and c-MYC). These AML-M5-derived iPSC showed features similar with those of human embryonic stem cells in terms of the morphology, gene expression, protein/antigen expression and differentiation capability. Parental-specific markers were down-regulated in these AML-M5-derived iPSCs. Expression of MLL-AF9 fusion gene (previously identified to be associated with pathogenesis of AML-M5) was observed in all iPSC clones as well as parental cells. We conclude that AML-M5-specific iPSC clones have been successfully developed. This disease model may provide a novel approach for future study of pathogenesis and therapeutic intervention of AML-M5.

**Keywords:** Acute monocytic leukemia, acute myeloid leukemia, induced pluripotent stem cells, MLL-AF9.

Synthesis of azomethines derived from cinnamaldehyde and vanillin: In vitro acetylcholinesterase inhibitory, antioxidant and insilico molecular docking studies

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Abstract

In the present study, we report the synthesis of azomethines derived from cinnamaldehyde (C1–C3) and vanillin (V1–V3) using ethanol as a green solvent in the presence of triethyl amine. The synthesized compounds were characterized and investigated for their free radical scavenging activity and anti-Alzheimer properties by DPPH and acetylcholinesterase (AChE) inhibition assays. The anti-Alzheimer properties of the compounds were determined by molecular docking and ADME predictions. Compounds, C1 and V1 were found to be potential with IC values of 0.01 ± 0.09 μM and 0.31 ± 0.03 μM respectively. The antioxidant activity of C1 in terms of DPPH and ABTS was found to be 16.22 ± 0.02 μM and 17.2 ± 0.02 μM, whereas V1 showed antioxidant activities at 14.07 ± 0.02 μM and 15.06 ± 0.03 μM respectively. In silico studies based on molecular docking and ADME predictions revealed the significance of azomethine derivatives as the potent anti-Alzheimer agents.

Keywords: Schiff bases, Cinnamaldehyde, Vanillin, Azomethines DPPH, Molecular docking, Acetylcholine esterase.
Assessment of knowledge of diabetes mellitus in the urban areas of Klang district, Malaysia

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Abstract
Diabetes is the most common cause of non-traumatic lower limb amputations and cardiovascular diseases. However, only a negligible percentage of the patients and subjects knew that the feet are affected in diabetes and diabetes affects the heart. Hence, a cross-sectional study was carried out to evaluate the knowledge of diabetes mellitus among the public of different age group, gender, ethnicity, and education level. A sample of 400 participants was randomly selected and data was collected using a structured questionnaire under non-contrived setting. The results showed that there is a statistically significant difference in knowledge on diabetes mellitus among different age groups and different ethnic origin but there is no significant difference in the knowledge among different gender and education level. Out of 400 respondents, 284 respondents (71%) knew that diabetes mellitus is actually a condition characterized by raised blood sugar. Age and education level of respondents were found to be the predominant predictive factors on diabetes knowledge, whereas the gender of respondents did not affect the findings of this study. An improved and well-structured educational programme that tackles the areas of weaknesses should be recommended to increase the level of knowledge on diabetes among Malaysians.

Keywords: diabetes mellitus, knowledge, cardiovascular disease, amputations.
Mandibular canal enlargement: Clinical and radiological characteristics

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Abstract
Enlargement of the mandibular canal is a rare radiological finding. Clinically, it may or may not be associated with sensory deficits. We report four cases of widening of the mandibular canal observed with various methods of imaging with different clinical characteristics. We describe this unique radiological finding and elaborate the importance of quality assessment of the imaging that is vital for accurate diagnosis and treatment planning. Clinicians should be mindful when assessing the imaging whenever the size of the mandibular canal is implicated. The case ranged from a benign tumor to malignancy, radiological errors, and artifacts. A more superior imaging or treatment modality was necessary to ascertain the diagnosis.

Keywords: Clinical characteristics, imaging characteristics, mandibular canal.

**Lutein improves cell viability and reduces Alu RNA accumulation in hydrogen peroxide challenged retinal pigment epithelial cells**

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**Abstract**

**Purpose:** Dysfunction of the microRNA (miRNA)-processing enzyme DICER1 and Alu RNA accumulation are linked to the pathogenesis of age-related macular degeneration (AMD). This study determined the optimal dose of lutein (LUT) and zeaxanthin (ZEA) to protect human retinal pigment epithelium (RPE) cells against hydrogen peroxide (H2O2). The effect of the optimal dose of LUT and ZEA as DICER1 and Alu RNA modulators in cultured human RPE cells challenged with H2O2 was investigated.

**Materials and methods:** ARPE-19 cells were pre-treated with LUT, ZEA, or both for 24 h before 200 μM H2O2 challenge. Cell viability was measured by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. DICER1 and Alu RNA were quantified by western blotting and real-time polymerase chain reaction, respectively.

**Results:** H2O2 increased cell Alu RNA expression and decreased cell viability of ARPE-19, but had no significant impact on the DICER1 protein level. LUT, alone and in combination with ZEA pre-treatment, prior to H2O2 challenge significantly improved cell viability of ARPE-19 and reduced the level of Alu RNA compared to the negative control.

**Conclusions:** These results support the use of LUT alone, and in combination with ZEA, in AMD prevention and treatment. This study is also the first to report LUT modulating effects on Alu RNA.

**Keywords:** Lutein, zeaxanthin, ARPE-19, DICER1, Alu RNA, age-related macular degeneration, hydrogen peroxide.
Pharmacokinetic and pharmacodynamic features of nanoemulsion following oral, intravenous, topical and nasal route

Hira Choudhury, Bapi Gorain, Bappaditya Chatterjee, Uttam K. Mandal, Pinaki Sengupta, Rakesh K. Tekade.

Abstract
Background: Most of the active pharmaceutical ingredients discovered recently in pharmaceutical field exhibits poor aqueous solubility that pose major problem in their oral administration. The oral administration of these drugs gets further complicated due to their short bioavailability, inconsistent absorption and inter/intra subject variability.

Methods: Pharmaceutical emulsion holds a significant place as a primary choice of oral drug delivery system for lipophilic drugs used in pediatric and geriatric patients. Pharmacokinetic studies on nanoemulsion mediated drugs delivery approach indicates practical feasibility in regards to their clinical translation and commercialization.

Results: This review article is to provide an updated understanding on pharmacokinetic and pharmacodynamic features of nanoemulsion delivered via oral, intravenous, topical and nasal route.

Conclusion: The article is of huge interest to formulation scientists working on range of lipophilic drug molecules intended to be administered through oral, intravenous, topical and nasal routes for vivid medical benefits.

Keywords: Hydrophobicity, oral delivery, pharmacokinetics, pharmacodynamics, routes of administration, carbon nanotubes.
Recent update on nanoemulgel as topical drug delivery system

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Abstract

Being an emerging transdermal delivery tool, nanoemulgel, has proved to show surprising upshots for the lipophilic drugs over other formulations. This lipophilic nature of majority of the newer drugs developed in this modern era resulting in poor oral bioavailability, erratic absorption, and pharmacokinetic variations. Therefore, this novel transdermal delivery system has been proved to be advantageous over other oral and topical drug delivery to avoid such disturbances. These nanoemulgels are basically oil-in-water nanoemulsions gelled with the use of some gelling agent in it. This gel phase in the formulation is nongreasy, which favors user compliance and stabilizes the formulation through reduction in surface as well as interfacial tension. Simultaneously, it can be targeted more specifically to the site of action and can avoid first-pass metabolism and relieve the user from gastric/systemic incompatibilities. This brief review is focused on nanoemulgel as a better topical drug delivery system including its components screening, formulation method, and recent pharmacokinetic and pharmacodynamic advancement in research studies carried out by the scientists all over the world. Therefore, at the end of this survey it could be inferred that nanoemulgel can be a better and effective drug delivery tool for the topical system.

Keywords: nanoemulgel, nanoemulsion, pharmacokinetic improvement, transdermal drug delivery.
Recent advances in TPGS-based nanoparticles of docetaxel for improved chemotherapy

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Abstract

Docetaxel (DTX) is one of the important antitumor drugs, being used in several common chemotherapies to control leading cancer types. Severe toxicities of the DTX are prominent due to sudden parenteral exposure of desired loading dose to maintain the therapeutic concentration. Field of nanotechnology is leading to resist sudden systemic exposure of DTX with more specific delivery to the site of cancer. Further nanometric size range of the formulation aid for prolonged circulation, thereby extensive exposure results better efficacy. In this article, we extensively reviewed the therapeutic benefit of incorporating \(d\)-\(\alpha\)-tocopheryl polyethylene glycol 1000 succinate (vitamin E TPGS, or simply TPGS) in the nanoparticle (NP) formulation of DTX for improved delivery, tumor control and tolerability. TPGS is well accepted nonionic-amphiphilic polymer which has been identified in the role of emulsifier, stabilizer, penetration enhancer, solubilizer and in protection in micelle. Simultaneously, Pglycoprotein inhibitory activity of TPGS in the multidrug resistant (MDR) cancer cells along with its apoptotic potential are the added advantage of TPGS to be incorporated in nanochemotherapeutics. Thus, it could be concluded that TPGS based nanoparticulate application is an advanced approach to improve therapeutic efficacy of chemotherapeutic agents by better internalization and sustained retention of the NPs.

Keywords: Nanoparticle, \(d\)-\(\alpha\)-tocopheryl polyethylene glycol 1000 succinate (TPGS), Docetaxel, Multi-drug resistance (MDR), Sustained release, Targeted delivery.
Development and validation of an LC-MS/MS-ESI method for comparative pharmacokinetic study of ciprofloxacin in healthy male subjects

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Abstract

A sensitive, specific and reproducible liquid chromatography coupled to tandem mass spectrometric method was developed and validated for the estimation of ciprofloxacin, an extensively used second-generation quinolone antibiotics, in human plasma. A liquid-liquid extraction of ciprofloxacin and the internal standard, ofloxacin, has been approached from the biological matrix using chloroform. Chromatographic separation was achieved in positive ion modes, isocratically on a 3.5 μm C18 analytical column (75 mm×4.6 mm, i.d.) with 0.2% formic acid solution in water: methanol (10:90, v/v) as mobile phase, at a flow rate of 0.5 mL.min⁻¹. The MS/MS ion transitions were monitored as 332.0→231.3 for ciprofloxacin and 362.2→261.0 for IS. The method showed good linearity in the range of 0.01–5.00 μg.mL⁻¹ (r² >0.99) with a good precision (3.37–12.60%) and accuracy (87.25–114%). At the same time, ciprofloxacin was found to be stable during stability studies viz. benchtop, auto-sampler, freeze-thaw cycle and long-term. The developed and validated method was successfully applied to measure plasma ciprofloxacin concentrations in a single dose bioequivalence study.

Keywords: ciprofloxacin, LC-MS/MS, bioequivalence study, human plasma, method validation.

Safety against nephrotoxicity in paclitaxel treatment: Oral nanocarrier as an effective tool in preclinical evaluation with marked in vivo antitumor activity

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Abstract

Oral paclitaxel (PTXL) formulations freed from cremophor® EL (CrEL) is always in utmost demand by the cancerous patients due to toxicities associated with the currently marketed formulation. In our previous investigation [Int. J. Pharm. 2014; 460:131], we have developed an oral oil based nanocarrier for the lipophilic drug, PTXL to target bioavailability issue and patient compliance. Here, we report in vivo antitumor activity and 28-day sub-chronic toxicity of the developed PTXL nanoemulsion. It was observed that the apoptotic potential of oral PTXL nanoemulsion significantly inhibited the growth of solid tumor (59.2 ± 7.17%; p < 0.001) without causing any explicit toxicity. The 6.5 mg/kg and 3 mg/kg oral PTXL nanoemulsion dose did not cause any notable alteration in haematological, biochemical/structural characteristics during 28-day sub-chronic toxicity studies in the experimental mice. Whereas, the toxicity of 12.8 mg/kg body weight dose showed decrease in RBC, haemoglobin and neutrophil counts. In contrast, marketed PTXL (Taxol®) was found to be comparatively more toxic to the experimental animals. Taxol® treatment resulted glomerulonephritis in histopathological examination, which could be correlated with increased level of creatinine and associated nephrotoxicity. This investigation concluded that the developed oral nanoemulsion presents a viable therapeutics bio-system to step towards clinical application as well as substitute CrEL based PTXL formulations.

Keywords: Antitumor activity, Hematological analysis, Histopathology, Oral nanoemulsion, Paclitaxel, Sub-chronic toxicity.
Herbal medicine, phytomedicine or botanical medicine are synonymous, utilizes plants intended for medicinal purposes. Medicinal use of herbal medicine in the treatment and prevention of diseases including diabetes has a long history compared to conventional medicine. Diabetes is one of the major public health concerns over the world. Diabetes or hyperglycemia is considered to be one of the common public health hazard; optimal control of which is still not possible. Persistent hyperglycemia or uncontrolled diabetes has the potential to cause serious complications such as kidney disease, vision loss, cardiovascular disease, and lower-limb amputations which contributed towards morbidity and mortality in diabetes. There are various approaches to treat and prevent diabetes as well as its secondary complications, one of it is herbal medicines. However, the selection of herbs might depends on several factors, which include the stage of progression of diabetes, types of comorbidities that the patients are having, availability, affordability as well as the safety profile of the herbs. This review focuses on the herbal and natural remedies that play the role in the treatment or prevention of this morbid disorder e diabetes, including their underlying mechanisms for the blood glucose-lowering property and the herbal products already been marketed for the remedial action of diabetes.

Keywords: Herbal medicine, Insulin secretion, Insulin resistivity, Active component, Diabetes control.

### Strategies to enhance production of microalgal biomass and lipids for biofuel feedstock

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**Abstract**

Microalgae have enormous potential as feedstock for biofuel production compared with other sources, due to their high areal productivity, relatively low environmental impact, and low impact on food security. However, high production costs are the major limitation for commercialization of algal biofuels. Strategies to maximize biomass and lipid production are crucial for improving the economics of using microalgae for biofuels. Selection of suitable algal strains, preferably from indigenous habitats, and further improvement of those 'platform strains' using mutagenesis and genetic engineering approaches are desirable. Conventional approaches to improve biomass and lipid productivity of microalgae mainly involve manipulation of nutritional (e.g. nitrogen and phosphorus) and environmental (e.g. temperature, light and salinity) factors. Approaches such as the addition of phytohormones, genetic and metabolic engineering, and co-cultivation of microalgae with yeasts and bacteria are more recent strategies to enhance biomass and lipid productivity of microalgae. Improvement in culture systems and the use of a hybrid system (i.e. a combination of open ponds and photobioreactors) is another strategy to optimize algal biomass and lipid production. In addition, the use of low-cost substrates such as agri-industrial wastewater for the cultivation of microalgae will be a smart strategy to reduce production costs. Such systems not only generate high algal biomass and lipid productivity, but are also useful for bioremediation of wastewater and bioremoval of waste CO2. The aim of this review is to highlight the advances in the use of various strategies to enhance production of algal biomass and lipids for biofuel feedstock.

**Keywords:** Biodiesel, biofuels, Chlorella, genetic engineering, microalgae, metabolic engineering.

**One-pot synthesis of cobalt incorporated polyglycerol ester as antimicrobial**

Bing Wei Chua, Choy Sin Lee, Wen Huei Lim, Mallikarjuna Rao Pichika.

**Abstract**

Cobalt-incorporated poly(glycerol ester) (Co–PGE) was synthesized by the polycondensation of glycerol and adipic acid followed by the reaction with cobalt(II) hydroxide under solvent-free and noncatalyzed one-pot synthesis conditions. The reaction was monitored through the acid value and hydroxyl value determination. The chemical structure and molecular weight of the poly(glycerol ester) (PGE) and Co–PGE were characterized by Fourier transform infrared spectroscopy, $^{13}$C-NMR, gel permeation chromatography, and inductively coupled plasma mass spectrometry. Co–PGE with a 59.3% degree of branching was incorporated with up to 5.0% w/w cobalt, and it exhibited antimicrobial inhibition against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Candida albicans* in a broth microdilution study. Polyurethane (PU) coatings were prepared by the blending of 0.5–35% w/w Co–PGE containing with 5% w/w of cobalt with blank PGE, poly(ethylene glycol) with a molecular weight of 6000, poly(caprolactone diol) with a molecular weight of 2000, and additives to react with isophorone diisocyanate. The prepared PUs demonstrated mild to high antimicrobial activities against *E. coli*, *S. aureus*, *Bacillus subtilis*, and *C. albicans* strains in a disc diffusion test. PU prepared with 0.5% w/w Co–PGE showed a mild inhibition activity against *S. aureus*, and PU prepared with 10% w/w Co–PGE demonstrated a high inhibition activity against *C. albicans*. This study demonstrated that value-added Co–PGE synthesized from glycerol has the potential as an antimicrobial agent for polymer coatings in biomedical devices.
Variant of Lemierre’s syndrome with internal jugular vein aneurysm

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Abstract
Internal jugular vein (IJV) aneurysm is a rare entity, and a thrombosed aneurysm poses diagnostic and management challenges. We came across a 53-year-old woman who presented with fever, vomiting and right neck swelling for a week. Laboratory investigations showed neutrophilic leucocytosis, raised acute phase reactant and blood culture yielded Klebsiella pneumoniae. Ultrasound and contrast-enhanced CT neck revealed a large fusiform aneurysm of the right IJV with filling defect extending from the aneurysm into the right transverse sinus. There was a cavity at the right lower third molar tooth. MRI confirmed the findings with additional enhancing focus at right lower periodontal region. The swelling reduced after 2 weeks of medical therapy, and follow-up imaging 4 months later showed complete resolution of the aneurysm with residual thrombosis. After extensive workup, dental infection remains the only identifiable primary source leading to thrombophlebitis of the right IJV and subsequent sequelae.

Keywords: dentistry and oral medicine, diabetes, ear, nose and throat/otolaryngology, infections.

Jerantinine A induces tumor-specific cell death through modulation of splicing factor 3b subunit 1 (SF3B1)

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Abstract

Precursor mRNA (pre-mRNA) splicing is catalyzed by a large ribonucleoprotein complex known as the spliceosome. Numerous studies have indicated that aberrant splicing patterns or mutations in spliceosome components, including the splicing factor 3b subunit 1 (SF3B1), are associated with hallmark cancer phenotypes. This has led to the identification and development of small molecules with spliceosome-modulating activity as potential anticancer agents. Jerantinine A (JA) is a novel indole alkaloid which displays potent anti-proliferative activities against human cancer cell lines by inhibiting tubulin polymerization and inducing G2/M cell cycle arrest. Using a combined pooled-genome wide shRNA library screen and global proteomic profiling, we showed that JA targets the spliceosome by up-regulating SF3B1 and SF3B3 protein in breast cancer cells. Notably, JA induced significant tumor-specific cell death and a significant increase in unspliced pre-mRNAs. In contrast, depletion of endogenous SF3B1 abrogated the apoptotic effects, but not the G2/M cell cycle arrest induced by JA. Further analyses showed that JA stabilizes endogenous SF3B1 protein in breast cancer cells and induced dissociation of the protein from the nucleosome complex. Together, these results demonstrate that JA exerts its antitumor activity by targeting SF3B1 and SF3B3 in addition to its reported targeting of tubulin polymerization.
Antimicrobial peptides as potential anti-biofilm agents against multidrug-resistant bacteria

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Abstract
Bacterial resistance to commonly used drugs has become a global health problem, causing increased infection cases and mortality rate. One of the main virulence determinants in many bacterial infections is biofilm formation, which significantly increases bacterial resistance to antibiotics and innate host defence. In the search to address the chronic infections caused by biofilms, antimicrobial peptides (AMP) have been considered as potential alternative agents to conventional antibiotics. Although AMPs are commonly considered as the primitive mechanism of immunity and has been extensively studied in insects and non-vertebrate organisms, there is now increasing evidence that AMPs also play a crucial role in human immunity. AMPs have exhibited broad-spectrum activity against many strains of Gram-positive and Gram-negative bacteria, including drug-resistant strains, and fungi. In addition, AMPs also showedsynergy with classical antibiotics, neutralize toxins and are active in animal models. In this review, the important mechanisms of action and potential of AMPs in the eradication of biofilm formation in multidrug-resistant pathogen, with the goal of designing novel antimicrobial therapeutics, are discussed.

Keywords: Antimicrobial peptide, Biofilms, Multidrug-resistant bacteria.

Current technology in the discovery and development of novel antibacterials

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Abstract

Bacterial resistance to antibiotics is one of the most serious challenges to global public health. The introduction of new antibiotics in clinical settings, i.e. agents that belong to a new class of antibacterials, act on new targets or has a novel mechanism of action, may not be sufficient to cope with the emergence of multidrug-resistant pathogens such as Staphylococcus aureus, Streptococcus pneumoniae, Pseudomonas aeruginosa, Klebsiella pneumoniae, Acinetobacter baumannii and Escherichia coli, which are increasingly prevalent in healthcare settings in Europe, the USA and Asia. Hence, coordinated efforts in minimizing the risk of spread of resistant bacteria and renewing research efforts in the search for novel antibacterial agents are urgently needed to manage this global crisis. With the explosion of bacterial genomic data and rapid development of new sequencing technologies, the understanding of bacterial pathogenesis and identification of novel antibiotic targets have significantly improved. This review highlights the challenges and potential in using current technologies in the discovery and development of novel antibacterial agents to keep up with the constantly evolving resistance in bacteria.

Keywords: high-throughput screening, multi-drug resistant bacteria, new generation sequencing, ‘omics’ technologies.

Plant-derived compounds as potential source of novel anti-biofilm agents against *Pseudomonas aeruginosa*

Pooi Yin Chung.

**Abstract**

*Pseudomonas aeruginosa* is the most common Gram-negative bacterium associated with nosocomial and life-threatening chronic infections in cystic fibrosis patients. This pathogen is well-known for its ability to attach to surfaces of indwelling medical devices to form biofilms, which consist of a regular array of extracellular polymers. Tenaciously bound to the surface of devices and inherently resilient to antibiotic treatment, *P. aeruginosa* poses a serious threat in clinical medicine and contributes to the persistence of chronic infections. Studies on microbial biofilms in the past decade involved mainly the understanding of environment signals, genetic elements and molecular mechanisms in biofilm formation, tolerance and dispersal. The knowledge obtained from the studies of these mechanisms is crucial in the establishment of strategies to eradicate or to prevent biofilm formation. Currently, biofilm infections are usually treated with combinations of antibiotics and surgical removal, in addition to frequent replacement of the infected device. More recently, specific natural sources have been identified as antibiofilm agents against this pathogen. This review will highlight the recent progress made by plant-derived compounds against *P. aeruginosa* biofilm infections in both in vitro or in vivo models.

**Keywords:** Anti-biofilm agents, *Pseudomonas aeruginosa*, plant-derived compounds.
A mini review on medicinal effects of edible bird’s nest

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Abstract
Edible bird’s nest is a famous and nutritious food which is well-known among Chinese community. It is made from the saliva of swiftlets. It is consumed for various reasons, including as health tonic, complexion enhancer, asthma alleviator and immune system enhancer. It contains both macronutrients and micronutrients such as carbohydrates, glycoproteins, calcium, sodium, magnesium, zinc, manganese, iron and others. To date, a number of studies have reported on the health benefits of EBN consumption. Hence, this review describes the various medicinal values of EBN.
Repatriation of human remains following death in international travelers

Ruairi Connolly, Richard Prendiville, Denis Cusack, Gerard Flaherty.

Abstract

Background: Death during international travel and the repatriation of human remains to one’s home country is a distressing and expensive process. Much organization is required involving close liaison between various agencies.


Results: The local national embassy, travel insurance broker and tour operator are important sources of information to facilitate the repatriation of the deceased traveller. Formal identification of the deceased's remains is required and a funeral director must be appointed. Following this, the coroner in the country or jurisdiction receiving the repatriated remains will require a number of documents prior to providing clearance for burial. Costs involved in repatriating remains must be borne by the family of the deceased although travel insurance may help defray some of the costs. If the death is secondary to an infectious disease, cremation at the site of death is preferred. No standardized procedure is in place to deal with the remains of a migrant’s body at present and these remains are often not repatriated to their country of origin.

Conclusions: Repatriation of human remains is a difficult task which is emotionally challenging for the bereaving family and friends. As a travel medicine practitioner, it is prudent to discuss all eventualities, including the risk of death, during the pre-travel consultation. Awareness of the procedures involved in this process may ease the burden on the grieving family at a difficult time.

Keywords: Repatriation, human remains, death, travel, tourism, travel insurance, International.
Mechanistic studies on the effect of *Nephelium lappaceum* seed powder on in vitro glucose uptake by *Saccharomyces cerevisiae*

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Abstract

We proposed to elucidate the antidiabetic potential of *Nephelium lappaceum* (Rambutan) seed powder (peeled and unpeeled) by using in vitro bioassay. In this study, we investigated the antidiabetic potential of rambutan seed powder using in vitro glucose uptake mechanism by Saccharomyces cerevisiae (yeast). Rambutan seed powder (unpeeled) at a test concentration of 25 mg/mL was remarkable to enhance glucose uptake by yeast cells. In summary, rambutan seed powder found to possesses in vitro yeast glucose uptake enhancing potential.

Keywords: Antidiabetic potential, Glucose uptake by yeast cells, *Nephelium lappaceum*, Rambutan.

**Differences of cutaneous two-point discrimination thresholds among students in different years of a chiropractic program**

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**Abstract**

**Objectives:** The aim of this study was to investigate if there were differences in the two-point discrimination (2-PD) of fingers among students at different stages of a chiropractic program.

**Methods:** This study measured 2-PD thresholds for the dominant and nondominant index finger and dominant and nondominant forearm in groups of students in a 4-year chiropractic program at the International Medical University in Kuala Lumpur, Malaysia. Measurements were made using digital calipers mounted on a modified weighing scale. Group comparisons were made among students for each year of the program (years 1, 2, 3, and 4). Analysis of the 2-PD threshold for differences among the year groups was performed with analysis of variance.

**Results:** The mean 2-PD threshold of the index finger was higher in the students who were in the higher year groups. Dominant-hand mean values for year 1 were 2.93 ± 0.04 mm and 1.69 ± 0.02 mm in year 4. There were significant differences at finger sites (P < .05) among all year groups compared with year 1. There were no significant differences measured at the dominant forearm between any year groups (P = .08). The nondominant fingers of the year groups 1, 2, and 4 showed better 2-PD compared with the dominant finger. There was a significant difference (P = .005) between the nondominant (1.93 ± 1.15) and dominant (2.27 ± 1.14) fingers when all groups were combined (n = 104).

**Conclusions:** The results of this study demonstrated that the finger 2-PD of the chiropractic students later in the program was more precise than that of students in the earlier program.

**Keywords:** Chiropractic, Touch, Touch Perception.

**Clinical and radiographic periodontal parameters and release of collagen degradation biomarkers in naswar dippers**

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**Abstract**

**Background and Objective:** The aim of the present study was to compare clinical periodontal parameters and to assess the release of C-telopeptides pyridinoline cross-links (ICTP) and C-terminal crosslinked telopeptide (CTX) from gingival collagen of naswar (NW) and non-naswar (control) dippers.

**Materials and Methods:** Eighty-seven individuals (42 individuals consuming NW and 45 controls) were included. Clinical (plaque index, bleeding on probing, probing depth and clinical attachment loss) and radiographic (marginal bone loss) periodontal parameters were compared among NW and control groups. Gingival specimens were taken from subjects in NW and control groups, assessed for ICTP and CTX levels (using ELISA) and analyzed using micro-Raman spectroscopy. The significance of differences in periodontal parameters between the groups was determined using Kruskal-Wallis and Mann-Whitney U tests. The percent loss of dry mass over exposure time and the rate of release of ICTP and CTX from all groups were compared using the paired t-test to examine the effects of exposure time.

**Results:** Clinical and radiographic periodontal parameters were significantly higher in the NW group than the control group (P < .01). In the Raman spectrum, the strongest and sharpest band occurred at 1260 cm\(^{-1}\) amongst NW users. A Raman band at Amide I was observed with slight shifts in wave numbers. The rate of ICTP and CTX release was significantly higher in subjects from the NW group compared with those from the control group (P < .05). Both factors, the type of groups and time, had a significant effect on release of ICTP and CTX (P < .05).

**Conclusion:** Within the limits of the present study, it may be concluded that clinical and radiographic periodontal parameters were worse among subjects in the NW group than in those of the control group. There is a higher degree of collagen breakdown in the connective tissue of subjects in the NW group as a result of naswar usage.

**Keywords:** collagen degradation, inflammation, periodontal disease, pyridinoline cross-links, smokeless tobacco.
Mechanical and spectroscopic analysis of retrieved/failed dental implants

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Abstract

The purpose of this study was to examine surface alterations and bone formation on the surface of failed dental implants (Straumann [ST] and TiUnite [TiUn]) removed due to any biological reason. In addition, failure analysis was performed to test mechanical properties. Dental implants (n = 38) from two manufacturers were collected and subjected to chemical cleaning. The presence of newly formed hydroxyapatite bone around failed implants was evaluated using micro-Raman spectroscopy. Scanning electron microscopy was used to identify surface defects. Mechanical testing was performed using a Minneapolis servo-hydraulic system (MTS) along with indentation using a universal testing machine and average values were recorded. A statistical analysis of mechanical properties was done using an unpaired t test, and correlation between observed defects was evaluated using Chi-square (p = 0.05). Apatite-formation was evident in both implants, but was found qualitatively more in the ST group. No significant difference was found in indentation between the two groups (p > 0.05). The percentage of “no defects” was significantly lower in the ST group (71%). Crack-like and full-crack defects were observed in 49% and 39% of TiUn. The ST group showed 11,061 cycles to failure as compared with 10,021 cycles in the TiUnite group. Implant failure mechanisms are complex with a combination of mechanical and biological reasons and these factors are variable with different implant systems.

Keywords: titanium, Raman, hydroxyapatite, failed, dental implant, mechanical, nanoindentation.
Awareness and use of electronic cigarettes: Perceptions of health science programme students in Malaysia


Abstract

Objectives: In recent years, electronic nicotine delivery systems (ENDS) or e-cigarettes appear to be gaining in popularity despite controversy over their health effects and public health impacts. This paper is the first in Malaysia to assess sociodemographic and behavioural characteristics associated with ENDS awareness, perceptions and use among students enrolled in health science programmes.

Design: Online self-reported use and perceptions of ENDS were assessed using a cross-sectional design.

Setting: The study was conducted at the International Medical University, Malaysia.

Method: An anonymous Internet-based, cross-sectional survey was conducted among a cohort of 404 undergraduate students at International Medical University, Malaysia, in September 2016. Data were collected over a period of 6 weeks. A 31-question web-based survey was developed to assess sociodemographic and behavioural characteristics associated with ENDS awareness, perceptions and use. Logistic regression analysis was performed to assess the impact of a set of predictors on e-cigarette use.

Results: Almost 95% of respondents were aware of e-cigarettes, 13.8% reported ever-use and students had varied perceptions towards e-cigarettes. Characteristics associated with greater likelihood of ever-use included gender, ethnicity and parents educational level. Other correlates included prior conventional cigarette smoking, prior hookah smoking, parents’ tobacco use and higher sensation-seeking behaviour total score.

Conclusion: In this sample of young adults, e-cigarette awareness was high and ever-use was evident especially among ever cigarette smokers. Nearly half of ever-users had not used an e-cigarette in the past 30 days of the survey and mostly reported flavoured over unflavoured e-cigarette use. These findings highlight the importance of e-cigarette surveillance and health promotion interventions targeting young adults.

Keywords: Awareness, cigarette smoking, e-cigarettes, Malaysia, sensation seeking, university students.
Molecular understanding of Epigallocatechin gallate (EGCG) in cardiovascular and metabolic diseases

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Abstract

Ethnopharmacological relevance: The compound epigallocatechin-3-gallate (EGCG), the major polyphenolic compound present in green tea [Camellia sinensis L. (Theaceae)], has shown numerous cardiovascular health promoting activity through modulating various pathways. However, molecular understanding of the cardiovascular protective role of EGCG has not been reported.

Aim of the review: This review aims to compile the preclinical and clinical studies that had been done on EGCG to investigate its protective effect on cardiovascular and metabolic diseases in order to provide a systematic guidance for future research.

Materials and methods: Research papers related to EGCG were obtained from the major scientific databases, for example, Science direct, PubMed, NCBI, Springer and Google scholar, from 1995 to 2017.

Results: EGCG was found to exhibit a wide range of therapeutic properties including antiatherosclerosis, anti-cardiac hypertrophy, anti-myocardial infarction, anti-diabetes, anti-inflammatory and antioxidant. These therapeutic effects are mainly associated with the inhibition of LDL cholesterol (anti-atherosclerosis), inhibition of NF-κB (anti-cardiac hypertrophy), inhibition of MPO activity (anti-myocardial infarction), reduction in plasma glucose and glycated hemoglobin level (anti-diabetes), reduction of inflammatory markers (anti-inflammatory) and the inhibition of ROS generation (antioxidant).

Conclusion: EGCG shows different biological activities and in this review, a compilation of how this bioactive molecule plays its role in treating cardiovascular and metabolic diseases was discussed.

Keywords: EGCG, diabetes, atherosclerosis, antioxidant, heart failure, anti-inflammatory.
A randomized cross-over study comparing the performance of HD integra™ central concentrate system versus pre-produced concentrate in hemodialysis

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Abstract

Background: Pre-produced bicarbonate concentrates (PPC) are still widely used in developing countries despite its cost and risk but Central Concentrate System (CCS) is lacking in data to support its wider adoption.

Methods: We conducted an 8-week randomized crossover study on 16 Hemodialysis machines to compare CCS versus PPC. Performance is assessed by solute concentrations while safety is assessed by microbial count, endotoxin level and adverse event reporting.

Results: Microbial counts and endotoxin levels were monitored on 48 occasions during the 8-week study for the CCS arm of the study. The levels were all below the action limit during the study. No patient reported any adverse events. Dialysate Sodium, Chloride and Bicarbonate concentrations were measured on a total of 128 occasions for each arm of the study. The relative deviations of Sodium, Chloride and Bicarbonate concentration were measured on a total of 128 occasions for each arm of the study. The 95% Confidence Intervals for the ratio of the mean solute concentrations on the CCS to PPC lie within the tolerance limit of ±5%.

Conclusion: Modern CCS is bacteriologically safe and its performance statistically equivalent to PPC.

Keywords: Chronic kidney disease, Dialysis, Dialysis fluid, Dialysate, Concentrate, Central concentrate system.
International travel and blood donation: Risks and restrictions

Gerard Flaherty, Brendan Moran, Patrick Higgins.

Abstract
Blood transfusion is an essential lifesaving therapy. However, it is not without its risks, including the risk of transmission of infectious disease. Standardized laboratory processes exist in blood donation services to avert this infectious risk. International travellers are potential blood donors who may inadvertently introduce infectious disease acquired abroad into their native country’s blood supply. This creates a significant challenge for blood banks whose duty it is to eliminate the risk of contamination of the blood supply with infectious agents. The donor deferral strategy utilizing a questionnaire-based screening approach is a standard mechanism for avoiding contamination of donated blood. It is relatively simple and cost effective as a screening tool. However, its main disadvantage is the potential shortfall in available.

Keywords: Blood donation, blood transfusion, international travel, infection.

**Individual traveller health priorities and the pre-travel health consultation**

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**Abstract**

The purpose of this study was to examine the principal travel health priorities of travellers. The most frequently selected travel health concerns were accessing medical care abroad, dying abroad, insect bites, malaria, personal safety and travel security threats. The travel health risks of least concern were culture shock, fear of flying, jet lag and sexually transmitted infections. This study is the first to develop a hierarchy of self-declared travel health risk priorities among travellers.

**Keywords:** Pre-travel consultation, patient communication, pre-travel risk assessment, travel health risks, travel history.

**Bibliometric analysis and curriculum mapping of travel medicine research**

Gerard T. Flaherty, Keng Lim Yap.

**Abstract**

Evidence-based travel medicine requires that research priorities reflect the wide knowledge base of this discipline. Bibliometric analysis of articles published in *Journal of Travel Medicine* yielded the following results: epidemiology (6%, \(n = 105\)); immunology/vaccinology (8.5%, \(n = 148\)); pre-travel assessment/consultation (30.5%, \(n = 533\)); diseases contracted during travel (48.3%, \(n = 843\)); other clinical conditions associated with travel (6.8%, \(n = 119\)); post-travel assessment (5.2%, \(n = 91\)) and administrative and general travel medicine issues (6%, \(n = 105\)).

**Keywords:** Bibliometric analysis, travel medicine, research, syllabus, Body of Knowledge, professional training.
Clinical audit training improves undergraduates’ performance in root canal therapy

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Abstract

Objectives: To evaluate the effectiveness of clinical audit as an educational tool in improving the technical quality of root canal treatment (RCT) and compliance with record-keeping performed by dental undergraduates.

Methods: Clinical audit learning was introduced in Year 3 of a five-year curriculum for dental undergraduates. During classroom activities, students were briefed on clinical audit, selected their audit topics in groups of five or six students, and prepared and presented their audit protocols. One chosen topic was RCT, in which three different groups of Year 3 students conducted retrospective audits of patients' records in 2012, 2014 and 2015 for their compliance with recommended record-keeping criteria and the technical quality of root canal fillings. Students were trained by and calibrated against an endodontist (kappa ≥ 0.8). After each audit the findings were reported in class and recommendations were made for improvement in performance of RCT and record-keeping. Students’ compliance with published guidelines is presented and their RCT performances in each year were compared using the chi-square test.

Results: Overall compliance with of record-keeping guidelines was 44.1% in 2012, 79.6% in 2014 and 94.6% in 2015 (p=0.001). In the 2012 audit, acceptable extension, condensation and no-mishap were observed in 75.7%, 69.1%, and 81.4%; in the 2014 audit, 64.8%, 95.1%, 51.4%; and in 2015 audit 81.9%, 96.4 % and 92.9% of cases respectively. In 2015, 76.8% of root canal fillings met all three technical quality criteria when compared to 48.6% in 2014 and 44.7% in 2012 (p=0.001).

Conclusions: Clinical audit is an effective educational tool for improving dental undergraduates’ compliance with record-keeping and performance in the technical quality of RCT.

**Random mutagenesis and precise gene editing technologies: Applications in algal crop improvement and functional genomics**

Sook Yee Gan & Christine A. Maggs.

**Abstract**
The establishment of a system for gene modification is crucial for the generation of new improved algal strains and elucidation of functional genome organization to enhance our understanding of algal biology. Several gene transfer methods have been developed for stable introduction of transgenes into algae allowing expression of desired foreign proteins. Site-specific gene integration and gene knockdown were achieved through homologous recombination and RNA interference approaches. The nuclease-associated gene editing technologies such as CRISPR-associated RNA-guided endonuclease Cas9 (CRISPR-Cas9) could efficiently generate stable targeted gene editing in algae. Although gene modification technologies have been established for algae, there are still practical difficulties that need to be addressed prior to commercialization such as transgene stability, potential risks and public acceptance. Genetic mitigation and containment strategies should be considered for commercial-scale production of transgenic algae.

**Keywords:** CRISPR-Cas9, gene knockdown, genetic transformation, insertional mutagenesis, reverse genetics, transgenic algae.

**Ultrasonic synthesis and in vitro evaluation of some new bischalcones as potential cytotoxic agents**

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**Abstract**

Despite the availability of various classes of chemotherapy agents for the treatment of the complicated disorder, cancer, developing most effective cytotoxic agents with high potency and least drawbacks being major concern in the field of medicinal chemistry. Therefore, the demand for novel molecules to treat cancer efficiently through multiple mechanisms is increasing. It is very much evident that bischalcones being the global research focus to compensate the demand. Fortunately, the development of the most appropriate bischalcone derivatives with high potency and binding affinity still not been addressed. Hence, emphasizing eco-friendly technological shift, in this research, ultrasonic technique was used to synthesis series of bischalcones derivatives, RVD1-RVD4. The potential cytotoxicity of the compounds was confirmed through in-vitro evaluation using Brine Shrimp (*Artemia salina*) Lethality Assay. Among the compounds tested, compound RVD3 and RVD4 has showed significant cytotoxicity at LD50 values 13.18 μg/mL ±0.12 and 13.80 μg/ml ±0.11 respectively. Consequently, in silico molecular docking studies have also been performed to evaluate the possible underlying mechanism of action of the compounds against Dihydrofolate Reductase enzyme (DHFR) anticancer drug target. Molecular docking results revealed that the highly potent bioactive bis-chalcone RVD3 is less selective towards inhibition of DHFR.

**Keywords:** Cancer, bis-chalcones, cytotoxic agent, ultrasonic, in-vitro brine shrimp (*Artemia salina*) lethality assay, molecular docking, Dihydrofolate Reductase (DHFR).
Application of diverse natural polymers in the design of oral gels for the treatment of periodontal diseases

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Abstract
The objective of this study was to prepare periodontal gels using natural polymers such as badam gum, karaya gum and chitosan. These gels were tested for their physical and biochemical properties and assessed for their antibacterial activity against Aggregatibacter actinomycetemcomitans and Streptococcus mutans, two pathogens associated with periodontal disease. Badam gum, karaya gum and chitosan were used to prepare gels of varying concentrations. Moxifloxacin hydrochloride, a known antimicrobial drug was chosen in the present study and it was added to the above gels. The gels were then run through a battery of tests in order to determine their physical properties such as pH and viscosity. Diffusion studies were carried out on the gels containing the drug. Antimicrobial testing of the gels against various bacteria was then carried out to determine the effectiveness of the gels against these pathogens. The results showed that natural polymers can be used to produce gels. These gels do not have inherent antimicrobial properties against A. actinomycetemcomitans and S. mutans. However, they can be used as a transport vehicle to carry and release antimicrobial drugs.
Significance of various experimental models and assay techniques in cancer diagnosis

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Abstract
The experimental models are of vital significance to provide information regarding biological as well as genetic factors that control the phenotypic characteristics of the disease and serve as the foundation for the development of rational intervention stratagem. This review highlights the importance of experimental models in the field of cancer management. The process of pathogenesis in cancer progression, invasion and metastasis can be successfully explained by employing clinically relevant laboratory models of the disease. Cancer cell lines have been used extensively to monitor the process of cancer pathogenesis process by controlling growth regulation and chemo-sensitivity for the evaluation of novel therapeutics in both in vitro and xenograft models. The experimental models have been used for the elaboration of diagnostic or therapeutic protocols, and thus employed in preclinical studies of bioactive agents relevant for cancer prevention. The outcome of this review should provide useful information in understanding and selection of various models in accordance with the stage of cancer.

Keywords: Animal models, cancer, cell lines studies, chemotherapy, in vitro models, in vitro studies.

**Selection of suitable endogenous reference genes for qPCR in kidney and hypothalamus of rats under testosterone influence**

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**Abstract**

Real-time quantitative PCR (qPCR) is the most reliable and accurate technique for analyses of gene expression. Endogenous reference genes are being used to normalize qPCR data even though their expression may vary under different conditions and in different tissues. Nonetheless, verification of expression of reference genes in selected studied tissue is essential in order to accurately assess the level of expression of target genes of interest. Therefore, in this study, we attempted to examine six commonly used reference genes in order to identify the gene being expressed most constantly under the influence of testosterone in the kidneys and hypothalamus. The reference genes include glyceraldehyde-3-phosphate dehydrogenase (GAPDH), actin beta (ACTB), beta-2 microglobulin (B2m), hypoxanthine phosphoribosyltransferase 1 (HPRT), peptidylprolyl isomerase A (Ppia) and hydroxymethylbilane synthase (Hmbs). The cycle threshold (Ct) value for each gene was determined and data obtained were analyzed using the software programs NormFinder, geNorm, BestKeeper, and rank aggregation. Results showed that Hmbs and Ppia genes were the most stably expressed in the hypothalamus. Meanwhile, in kidneys, Hmbs and GAPDH appeared to be the most constant genes. In conclusion, variations in expression levels of reference genes occur in kidneys and hypothalamus under similar conditions; thus, it is important to verify reference gene levels in these tissues prior to commencing any studies.
Analysis of high caesarean section rates: the second step after audits using the Ten Group Classification System

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Abstract
Objective: To identify possible methods of reducing high caesarean section rates in a tertiary care hospital.

Method: Analysis of birth weight of neonates, maternal age and indications for caesarean section in the groups identified by a modification of Robson’s 10 Group Classification of caesarean section (TGCS), which contribute significantly to the high caesarean section rates in the University Obstetric Unit, Teaching Hospital Mahamodara, Galle Sri Lanka during 2010 - 2014.

Results: Among nulliparous women, at term, having a singleton fetus, with a vertex presentation (NTSV) who underwent a caesarian section 25.6% delivered neonates weighing between 2500g and 2999g. Among multiparous women, at term, with no previous caesarean section, having a singleton fetus with a vertex presentation (MTSV) who underwent a caesarian section, those delivering neonates weighing between 2500g and 2999g ranged from 25.6% to 34.6%. Indications for ante partum caesarean section included fetal distress, subfertility, increased maternal age and cephalo-pelvic disproportion in NTSV, and fetal distress, vaginal varices, and a bad obstetric history in MTSV. Among multiparous women with one previous caesarean section undergoing repeat caesarean section, 29.8% delivered neonates weighing between 2500g and 2999g. Women >35 years had a higher risk of caesarean section, irrespective of whether they were nulliparous or multiparous, and whether they had a previous caesarean section or not.

Conclusion: A reduction in caesarean section rates in NTSV and MTSV, and women with one previous caesarean section, especially in those with foetuses weighing 2500g - 2999g, should be considered. Increased maternal age and subfertility per se should not be routine indications for antepartum caesarean section. Antepartum caesarean section for vaginal varices and cephalo-pelvic disproportion should be avoided. The diagnosis of fetal distress should be improved.
The use of nanoscaffolds and dendrimers in tissue engineering

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Abstract

To avoid tissue rejection during organ transplantation, research has focused on the use of tissue engineering to regenerate required tissues or organs for patients. The biomedical applications of hyperbranched, multivalent, structurally uniform, biocompatible dendrimers in tissue engineering include the mimicking of natural extracellular matrices (ECMs) in the 3D microenvironment. Dendrimers are unimolecular architects that can incorporate a variety of biological and/or chemical substances in a 3D architecture to actively support the scaffold microenvironment during cell growth. Here, we review the use of dendritic delivery systems in tissue engineering. We discuss the available literature, highlighting the 3D architecture and preparation of these nanoscaffolds, and also review challenges to, and advances in, the use dendrimers in tissue engineering. Advances in the manufacturing of dendritic nanoparticles and scaffold architectures have resulted in the successful incorporation of dendritic scaffolds in tissue engineering.
Swimming against the tide in STEM education and gender equality: A problem of recruitment or retention in Malaysia

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Abstract
Science, technology, engineering and mathematics (STEM) is acknowledged as one of the key drivers of technological innovation. Malaysian women join the educational pipeline as equals to their male counterparts. Nevertheless, women are persistently under-represented in technology and engineering, but over-represented in other STEM fields. Using data provided by the Malaysian Ministry of Higher Education, our results suggest that under-representation of women in engineering was attributed to low recruitment at the point of entry. Such a finding thus begs the question as to why women were not recruited into engineering. Malaysian policymakers and educators need to address under-representation of women in order to achieve gender equality in STEM, as part of the goals of Millennium Development and Vision 2020; to become a nation that is competent, confident and innovative in harnessing and advancing science and technology.

Keywords: STEM, gender gap, education, representation, retention.
Gupta ED, Ng WR, Wong SF, Bhurhanudeen AK, Yeap SS. Correlation of serum cartilage oligomeric matrix protein (COMP) and interleukin-16 (IL-16) levels with disease severity in primary knee osteoarthritis: A pilot study in a Malaysian population. PLoS One, 2017; 12(9): e0184802. doi: 10.1371/journal.pone.0184802. (ISI IF: 3.234; CiteScore: 3.32; Tier: Q1).

**Correlation of serum cartilage oligomeric matrix protein (COMP) and interleukin-16 (IL-16) levels with disease severity in primary knee osteoarthritis: A pilot study in a Malaysian population**

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**Abstract**

**Objective:** The aim of this study was to investigate the correlations between serum cartilage oligomeric matrix protein (COMP), interleukin-16 (IL-16) and different grades of knee osteoarthritis (KOA) in Malaysian subjects.

**Methods:** Ninety subjects were recruited comprising 30 with Kellgren-Lawrence (K-L) grade 2 KOA, 27 with K-L grade 3 KOA, 7 with grade 4 KOA, and 30 healthy controls. All subjects completed the Western Ontario and McMaster Universities Arthritis Index (WOMAC) questionnaire. Serum COMP and IL-16 levels were measured using ELISA and their values log transformed to ensure a normal distribution.

**Results:** There was no significant differences in levels of log serum COMP and IL-16 between healthy controls and KOA patients. There were no significant differences in the log serum COMP and IL-16 levels within the different K-L grades in the KOA patients. In KOA patients, log serum IL-16 levels significantly correlated with the WOMAC score (p = 0.001) and its subscales, pain (p = 0.005), stiffness (p = 0.019) and physical function (p<0.0001). Serum IL-16 levels were significantly higher in Malaysian Indians compared to Malays and Chinese (p = 0.024).

**Conclusions:** In this multi-ethnic Malaysian population, there was no difference in serum COMP and IL-16 levels between healthy controls and patients with KOA, nor was there any difference in serum COMP or IL-16 levels across the various K-L grades of KOA. However, there were significant inter-racial differences in serum IL-16 levels.
Pharmacological evaluation of the recuperative effect of morusin against aluminium trichloride (AlCl3)- induced memory impairment in rats

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Abstract

Background: Elevation in brain levels of aluminium can be neurotoxic and can cause learning and memory deficiencies. In Chinese medicine, Morus alba is used as a neuroprotective herb. The current study was intended to discover the recuperative effect of morusin against aluminium trichloride (AlCl3)-induced memory impairment in rats along with biochemical mechanism of its protective action.

Methods: Memory deficiency was produced by AlCl3 (100 mg/kg; p.o.) in experimental animals. Learning and memory activity was measured using Morris water maze (MWM) test model. Central cholinergic activity was evaluated through the measurement of brain acetylcholinesterase (AChE) activity. In addition to the above, oxidative stress was determined through assessment of brain thiobarbituric acid-reactive species (TBARS) and glutathione (GSH) levels.

Results: AlCl3 administration prompted significant deficiency of learning and memory in rats, as specified by a noticeable reduction in MWM presentation. AlCl3 administration also produced a significant deterioration in brain AChE action and brain oxidative stress (increase in TBARS and decrease in GSH) levels. Treatment with morusin (5.0 and 10.0 mg/kg, dose orally) significantly overturned AlCl3-induced learning and memory shortages along with diminution of AlCl3-induced rise in brain AChE activity and brain oxidative stress levels.

Conclusion: It may be concluded that morusin exerts a memory-preservative outcome in mental discrepancies of rats feasibly through its various activities.

Keywords: Acetylcholinestrase, AlCl3, aluminium trichloride, glutathione, morusin, thiobarbituric acid.
Tumor suppressor role of miR-503

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Abstract

MicroRNAs (miRNAs) are noncoding RNAs of around 20-25 nucleotides in length with highly conserved characteristics. They moderate posttranscriptional silencing by precisely combining with 3' untranslated regions (UTRs) of target mRNAs at a complementary site. miR503, an associate of the "canonical" miRNA16 family, is expressed in numerous types of tumors such as breast cancer, prostate cancer, lung cancer, colorectal cancer, hepatocellular carcinoma, glioblastoma and several others. There is convincing evidence to show that miR503 functions as a tumor suppressor gene through its effects on target genes that regulate cell proliferation, migration, and invasion in tumor cells. In this current assessment, we discuss the biology and tumor suppressor role of miR503 in different cancers and elaborate on its mechanism of action.

**Nephrotoxicity in rats exposed to paracetamol: The protective role of moralbosteroid, a steroidal glycoside**

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**Abstract**

Paracetamol (PCM) has an acceptable safety profile when used at prescribed doses. However, it is now understood that paracetamol can damage the kidneys when administered as an overdose. In addition, oxidative stress can play a major role in causing nephrotoxicity. This investigation studies the efficacy of moralbosteroid isolated from M. alba stem bark. Nephrotoxicity was induced with administration of paracetamol. Nephroprotection was studied using two doses of the extract. The experimental animals were divided into four groups (n = 6). Two groups served as positive and negative controls, respectively, and two received the test substances. All of the contents were orally administered. Significant reductions in nephrotoxicity and oxidative damages were observed in the treatment groups. There was a marked decrease in blood levels of urea, creatinine, and lipid peroxidation. Furthermore, it was found that glutathione levels in the blood increased dramatically after treatment. Histological findings confirmed the potent renoprotective potential of moralbosteroid. This was evidenced by the minimized intensity of nephritic cellular destruction. In animal studies, moralbosteroid exhibited dose-dependent activity, which is thought to be mediated through its antioxidant potential.
Intranasal drug delivery: A non-invasive approach for the better delivery of neurotherapeutics

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Abstract

Background: The convoluted pathophysiology of brain disorders along with penetration issue of drugs to brain represents major hurdle that requires some novel therapies. The blood-brain barrier (BBB) denotes a rigid barrier for delivery of therapeutics in vivo, to overcome this barrier intranasal delivery is an excellent strategy to deliver the drug directly to brain via olfactory and trigeminal nerve pathways that originate as olfactory neuro-epithelium in the nasal cavity and terminate in brain.

Methods: Kind of therapeutics like low molecular weight drugs can be delivered to the CNS via this route. In this review we have outlined the anatomy and physiological aspect of nasal mucosa, certain hurdles, various strategies including importance of muco-adhesive polymers to increase the drug delivery and possible clinical prospects that are partly contribute in intranasal drug delivery.

Results: Exhaustive literature survey related to intranasal drug delivery system revealed the new strategy that circumvents the BBB, based on non-invasive concept for treating various CNS disorders. Numerous advantages like prompt effects, self-medication through wide-ranging devices, and the frequent as well protracted dosing are associated with this novel route.

Conclusion: Recently few reports have proved that nasal to brain drug delivery system that bypasses the BBB. This novel route associated with targeting efficiency and less exposure of therapeutic substances to non-target site. Nevertheless, this route desires much more research into the safe transferring of therapeutics to the brain. Role of muco-adhesive polymer and surface modification with specific ligands are area of interest of researcher to explore more about this.

Keywords: Blood-brain barrier, CNS, Dosage form, Intranasal delivery, Mucoadhesive, Neurotherapeutics.
Hasan SS, Kow CS, Thiruchelvam K, Chong DWK, Ahmed SI. An evaluation of central nervous system (CNS) medication use and frailty among residents of aged care homes in Malaysia. *Neuroepidemiology*, 2017; 49(1-2): 82-90. (ISI IF: 2.886; CiteScore: 3.12; Tier: Q1).

An evaluation of central nervous system (CNS) medication use and frailty among residents of aged care homes in Malaysia

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**Abstract**

**Background/Aims:** Old age and institutionalization in care homes are associated with increased use of risk medications affecting the central nervous system (CNS). This study evaluated medication utilization and appropriateness; and assessed frailty among residents of Malaysian aged care homes.

**Methods:** The subjects of this study included 202 elderly (≥65 years) residents of 17 aged care homes in suburban peninsular Malaysia. Frailty was measured using the Groningen Frailty Indicator (GFI) score and independence in daily living was measured as KATZ activity of daily living score. Medication appropriateness was assessed using the Medication Appropriateness Index (MAI) and 2015 Beers' criteria for Potentially Inappropriate Medication (PIM).

**Results:** CNS medications constituted about 16% of the total, with an average of 0.8 ± 1.1 medications per resident, which reduced to 0.5 ± 0.8 medications after 3 months. Frailty (154/202) and polypharmacy (90/202) were highly prevalent in study subjects. Subjects on CNS medications had significantly higher GFI score (7.1 vs. 5.9; p = 0.031), polypharmacy (57.8 vs. 35.3%; p = 0.002), number of PIMs (0.9 vs. 0.2; p = 0.001), and mean summed MAI score (3.6 vs. 2.6; p = 0.015) than subjects not on CNS medications. Medication number was also significantly correlated with GFI (r = 0.194; p = 0.006) and KATZ (r = 0.141; p = 0.046) scores.

**Conclusion:** Frailty and polypharmacy were highly prevalent among aged care home subjects taking CNS medications. These findings support the notion that periodic regular medication review should improve the overall use of medications in elderly patients.

**Keywords:** Aged care, Central nervous system, Elderly care, Frailty, Medication appropriateness.
An evaluation of medication appropriateness and frailty among residents of aged care homes in Malaysia: A cross-sectional study


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Abstract
Aging is significantly associated with the development of comorbid chronic conditions. These conditions indicate the use of multiple medications, and are often warranted by clinical guidelines. The aim of the present study was to evaluate medication appropriateness and frailty among Malaysian aged care home residents with chronic disease. The participants were 202 elderly (≥65 years) individuals, a cross-sectional sample from 17 aged care homes. After ethics approval, each participant was interviewed to collect data on sociodemographics, frailty status (Groningen Frailty Indicator [GFI]), medication appropriateness (Medication Appropriateness Index [MAI]), the 2015 Beers’ criteria (Potentially Inappropriate Medication [PIM]), and 2014 STOPP criteria (Potentially Inappropriate Prescribing [PIP]). The findings show that 81% (n=164) and 42% (n=85) were taking medications for cardiovascular and central nervous system-related conditions, respectively, and 34% were using medications for diabetes (n=69). Each participant had a mean of 2.9±1.5 chronic diseases, with an average GFI score of 6.4±3.6. More than three-quarters of the participants (76%) were frail and polypharmacy was a factor in nearly half (48%); 41% and 36% were prescribed at least one PIP and PIM, respectively, whereas the average MAI score was 0.6 (range: 0–6). The number of medications used per participant correlated significantly and positively (0.21, P=.002) with GFI score. These findings reinforce the need for participants of aged care homes to receive periodic medication review aimed at minimizing morbidity associated with inappropriate pharmacotherapy.

Keywords: aged care, chronic diseases, elderly, frailty, medication appropriateness.

**Simulation-based instruction for pharmacy practice skill development: A review of the literature**

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**Abstract**

**Background:** Simulation is attractive for its potential for applying a control over learning environment, content complexity, teacher time, costs and risk. Simulation-based instruction (SBI) is poised to expand in pharmacy practice and education. This systematic review synthesises published, SBI in first-degree pharmacy programmes, especially those pertaining to psychomotor or cognitive skill development.

**Materials and Methods:** MEDLINE, Cumulative Index to Nursing and Allied Health Literature, and some education journals were searched for relevant articles published between January 2000 and December 2015.

**Results:** Of 108 articles identified, 12 were included, which were covering four major simulation-based interventions. These simulation-based interventions were diverse, and they covered a range of competencies and outcome measures. Nine studies included medication, and five studies included physical examination/procedure-related competencies as outcome measures. The evidence from nine studies suggested that skills could be improved through interventions involving human patient simulation.

**Conclusion:** Despite improvements in students’ ability to perform, there is a lack of evidence on how this translates to real settings and to patient satisfaction.

**Keywords:** Cognitive, instruction, pharmacy, psychomotor, simulation, skills.

**Economic evaluation of pharmacist-led medication reviews in residential aged care facilities**

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**Abstract**
Medication reviews is a widely accepted approach known to have a substantial impact on patients’ pharmacotherapy and safety. Numerous options to optimise pharmacotherapy in older people have been reported in literature and they include medication reviews, computerised decision support systems, management teams, and educational approaches. Pharmacist-led medication reviews are increasingly being conducted, aimed at attaining patient safety and medication optimisation. Cost effectiveness is an essential aspect of a medication review evaluation. Areas covered: A systematic searching of articles that examined the cost-effectiveness of medication reviews conducted in aged care facilities was performed using the relevant databases. Pharmacist-led medication reviews confer many benefits such as attainment of biomarker targets for improved clinical outcomes, and other clinical parameters, as well as depict concrete financial advantages in terms of decrement in total medication costs and associated cost savings. Expert commentary: The cost-effectiveness of medication reviews are more consequential than ever before. A critical evaluation of pharmacist-led medication reviews in residential aged care facilities from an economical aspect is crucial in determining if the time, effort, and direct and indirect costs involved in the review rationalise the significance of conducting medication reviews for older people in aged care facilities.

**Keywords:** Pharmacoeconomics, agedcare facilities, health economics, pharmacist, pharmacy.
Effects of Situation, Background, Assessment, and Recommendation (SBAR) usage on communication skills among nurses in a private hospital in Kuala Lumpur

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Abstract

Background: Situation, Background, Assessment and Recommendation (SBAR) is a standardized communication tool used to enhance patients' safety and quality of care in the hospital.

Aim and Objectives: The objective of this study was to determine the effects of Situation, Background, Assessment, and Recommendation (SBAR) usage on the communication skills among nurses in a private hospital in Kuala Lumpur.

Material and Methods: A cross-sectional descriptive study was conducted with 189 respondents who fulfilled the inclusion criteria. A set of questionnaires related to communication using SBAR was adapted and scored using a 5-point Likert scale.

Results: The mean total score of communication was (M = 25.63, SD= 6.74) which indicated moderate level. There were significant differences between marital status of respondents with communication level of married (M=30.26, SD=7.29) and unmarried (M = 22.04, SD = 7.85) with (t=-7.95, p<0.01). There was likewise, significant difference found between higher diploma respondents (M = 30.26, SD = 5.19) (M = 24.76, SD = 7.99) and diploma with (t=-4.82, p<0.01). In terms of designation, communication level was higher among charge nurses (M = 29.50, SD = 5.73) than registered nurses (M = 24.12, SD = 7.98) with (t=-3.19, p<0.01).

Conclusion: Effective communication through the use of SBAR is associated with the marital status, education level, and designation of nurses in the private hospital.

Keywords: Nurse, Communication, Situation-Background-Assessment-Recommendation (SBAR).
Pharmacokinetic changes in congestive heart failure

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Abstract
Pharmacokinetic processes are recognized as “liberation, absorption (A), distribution (D), metabolism (M) and excretion (E)”. Published ADME data for each drug are usually observed on healthy individuals. It serves as an indispensable guide to prescribers. LADME guides highlight the significant role of the gastroenterology system, hepatobiliary system, cardiovascular system and renal system. Any changes in the structure and function of these systems would lead to variations in the ADME system. The existence of individual differences and pathophysiological status of major organs further affects the clinical pharmacokinetic profile of drugs. Therefore, unpredictable variations in pharmacokinetic parameters may exist in patients suffering from diseases of the heart, the liver or the kidneys. Most importantly, the deviation of pharmacokinetic parameters could affect the outcome of the management of the disease. Of these organs, the heart is a very crucial one as the circulation is the main transport route for the passage of drugs through the body. Congestive heart failure is a common cardiac disease in both the well-developed and the developing countries. The pathophysiology of congestive heart failure has already been complicated with hemodynamic abnormalities, neurohumoral mechanisms and the damage to the cardiac muscle itself. As congestive heart failure is more commonly seen in the elderly patients, age-related changes should also be considered. The objective of this article is to facilitate the better management of congestive heart failure, based on evidence-based information on pharmacokinetic changes, to make dosage adjustment of the right drug for the right patient, with minimal adverse effects.

Keywords: clinical pharmacokinetic, congestive heart failure, pharmacokinetic changes, drug metabolism, drug absorption, drug elimination.

**Herbs for effective treatment of diabetes mellitus: medicinal chemistry and future therapeutic options**

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**Abstract**

The incidence of diabetes mellitus (DM) has increased globally. Various complications such as blindness, nephropathy leading to renal failure, neuropathy, foot ulceration, amputation, and disturbance in autonomic nervous system have been reported. Although, allopathy treatment still remains the treatment of choice, there is a need to look at the easy availability, patient compliance and cheaper cost of the drugs used in day-day practice. In this regard, complementary and alternative medicine has a greater role to play. Numerous plant extracts have been shown to exhibit antihyperglycemic properties. In the present review, we discuss the possible mechanism of wound healing in DM with regard to advanced glycation end products, inflammation, macrophages, non-leukocytic cells such as keratinocytes, fibroblasts and endothelial cells, matrix metalloproteinase and miRNA. We also discuss the various active compounds present in different plant extracts which may prove to be beneficial in DM. The review opens the door for effective treatment of DM wounds with plant extracts and plan future treatment options.

**Keywords:** Diabetes mellitus, active compounds, healing, treatment, wound.
The modified Gompertz model demonstrates a variable growth rate between two *Centella asiatica* phenotypes

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Abstract

*Centella asiatica*, a weakly aromatic plant that flourishes in wet tropical and sub-tropical areas as a medicinal species since ancient times. It contained important terpenoids that impart important medicinal values. Currently, studies on the terpenoid content of various *Centella asiatica* phenotypes have shown not only variable content but variable growth rates of different phenotypes that can affect future selection of phenotypes. The use of mathematical growth modelling can reveal important growth constants and discriminate between faster and slower growth phenotypes. Two *Centella asiatica* phenotypes from South Africa is modelled using the modified Gompertz model and the results showed that the *C. asiatica* Type-1 exhibited a faster growth rates and a shorter lag period at 0.152 day\(^{-1}\) and 2.313 day than another phenotype; *C. asiatica* Type 2 with a growth rate and a lag period of 0.067 day\(^{-1}\) and 3.363 day, respectively. The data indicates that different phenotypes of *C. asiatica* can have different growth rates and lag period and this can be important for selection of phenotypes to be used as the best bioactive peptides producer.

Keywords: *Centella asiatica*, phenotypes, modified Gompertz, growth rate, lag period.

**Comparative effectiveness of oral iron medications and patient preference in anemia during pregnancy**

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**Abstract**

**Objectives:** This study was design to compare the efficacy and patient preference of three different marketed formulations as folic acid plus ferrous fumarate, or carbonyl iron or amino acid plus chelated iron in the treatment of anemia during pregnancy.

**Materials and methods:** The study was multi-centric, randomized and controlled. Patients with 15-25 weeks of pregnancy with hemoglobin between 6 to 10 g/dl were included in this study. The enrolled 156 patients were randomly allocated to received folic acid plus ferrous fumarate, or carbonyl iron or amino acid plus chelated iron, once daily for a period of 12 weeks. Hemoglobin was estimated at baseline, 6 weeks and at the 12 weeks of the treatment.

**Results:** At the end of treatment the hemoglobin of the patients in the folic acid plus ferrous fumarate group achieved the WHO target, 11.2 ± 1.7 as compared to the carbonyl iron group 9.93 ± 0.82 and the amino acid plus chelated iron group 9.82 ± 0.65 (p>0.05). The serum ferritin level at the end of treatment in the ferrous fumarate plus folic acid group were reached 25.65 ± 4.61 whereas the patients in the carbonyl iron group reached 22.20 ± 1.7 and in the amino acid plus chelated iron group reached up to 21.36 ± 0.98 (p>0.05). More adverse effects occur in the carbonyl iron group patients.

**Conclusion:** Folic acid plus ferrous fumarate is superior in efficacy, safe in pregnancy and better preferred as compare to carbonyl iron or amino acid plus chelated iron and gives a good hematological response with minimal adverse effects.

**Keywords:** Iron deficiency anemia, pregnant women, folic acid, ferrous fumarate, carbonyl iron and amino acid.

**A 15-year single center retrospective study of antiphospholipid syndrome patients from northern Malaysia**

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**Abstract**

**Background:** Antiphospholipid syndrome (APS) is an autoimmune disorder characterised by thrombosis and/or pregnancy morbidity in the presence of antiphospholipid antibodies (aPLs) based on the Sydney criteria. We aimed to explore the clinico-laboratory features and treatment strategies of APS patients retrospectively.

**Methodology:** The medical records of APS patients registered under Hospital Universiti Sains Malaysia (Kelantan state) between 2000 and 2015 were reviewed.

**Results:** A total of 17 APS subjects (age 40.7 ± 12.8 years) including 11 primary (64.7%) and six secondary APS (35.3%) patients were identified. The follow-up period was 9.5 ± 6.7 years with male: female ratio of 1.0:4.7. Pregnancy morbidity was the most common clinical manifestation (11/14; 78.6%) followed by recurrent venous thrombosis (10/17; 58.8%). For other clinical features, menorrhagia was the most frequently observed manifestation (4/14; 28.6%) followed by aPLs-associated thrombocytopenia (4/17; 23.5%) and ovarian cyst (3/14; 21.4%). LA and aCL were positive in 94.1% (16/17) and 81.8% (9/11) of the patients, respectively. APTT value (76.7 ± 17.0 sec) was significantly high (p < 0.05). Low intensity warfarin alone was successful to maintain target INR (2.0 - 3.0) and prevent recurrence of thrombosis.

**Conclusion:** The tendency of pregnancy morbidity in this cohort of Malaysian Kelantanese APS patients was high compared to other previously reported APS cohorts. Low intensity warfarin was successful in preventing recurrence of thrombosis, however, APS women receiving long-term anticoagulants should be monitored for possible occurrence of menorrhagia and ovarian cysts.

**Keywords:** antiphospholipid syndrome, antiphospholipid antibodies, pregnancy morbidity, menorrhagia, ovarian cyst, anticoagulants, retrospective study.

Presence of anticardiolipin antibodies in patients with dementia: A systematic review and meta-analysis

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Abstract

Growing evidences are supporting towards the involvement of antiphospholipid antibodies [aPLs e.g., lupus anticoagulant (LA), anticardiolipin (aCL) and anti-β2-glycoprotein I (anti-β2-GPI) antibodies] in various neurological manifestations including migraine, epilepsy and dementia in the presence or absence of autoimmune diseases such as antiphospholipid syndrome or systemic lupus erythematosus. The aim of this systematic review and meta-analysis was to assess the presence of aPLs in dementia patients without a diagnosis of any autoimmune disease. Electronic databases (e.g., PubMed, Web of Science, Scopus, ScienceDirect and Google Scholar) were searched without any year or language restrictions and based on the inclusion criteria, nine prospective case-control studies assessing only aCL were included involving 372 dementia patients and 337 healthy controls. No studies were found to assess the presence of both LA or anti-β2-GPI. The study-specific odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using random-effects model. We observed the prevalence of aCL in dementia was higher (32.80%) than that of controls (9.50%) e.g., 3.45 times higher risk of presenting with dementia than the controls, and significant presence of aCL antibodies was detected in dementia patients compared to controls (OR: 4.94, 95% CI: 2.66 – 9.16, p < 0.00001; I² = 32%, p = 0.16). Publication bias was not observed from Egger’s (p = 0.081) and Begg’s tests (p = 0.180). Based on the study quality assessment using modified Newcastle–Ottawa Scale for case-control studies, seven of nine studies were of high methodological quality scoring ≥ 7 (median value). In summary, aCL antibodies were significantly present in dementia patients suggesting that aCL antibodies are generated due to the autoimmune-derived effects of dementia or there might be a potential causative role of this autoantibody in dementia pathogenesis.

Keywords: dementia, Alzheimer’s disease, antiphospholipid antibodies, anticardiolipin antibodies, systematic review, meta-analysis.
Abstract

Tuberous sclerosis complex (TSC) is an autosomal dominant neurocutaneous disorder characterized by tumor growth in multiple organs and caused by mutations in either TSC1 or TSC2 genes. Because of their relatively large genomic sizes, absence of hotspots, and common type of mutations, mutation detection in TSC1 and TSC2 genes has been challenging. We devised a combination of multiple ligation-dependent probe amplification (MLPA) and amplicon sequencing (AS) to simplify the detection strategy, yet we came up with a reasonably high detection rate. Thirty-four Malaysian patients diagnosed with TSC were referred to Human Genome Center, Universiti Sains Malaysia. We used a combination of MLPA to detect large copy number changes and AS to detect smaller mutations. TSC1 pathogenic or likely pathogenic mutations were found in 6 patients (18%) and TSC2 in 21 patients (62%), whereas 6 patients (18%) showed no mutations and 1 patient (2%) showed only TSC2 missense variant with uncertain significance. Six of the mutations are novel. Our detection strategy costs 81% less and require 1 working week less than the conventional strategy. Confirmatory sequencing using Sanger method on a few representative mutations showed agreement with results of the AS. Combination of MLPA and Illumina MiSeq AS provides a simplified strategy and reasonably high detection rate for TSC1/TSC2 mutation, which suggested application of the strategies into clinical molecular diagnostics.
Protective effect of magnesium acetyltaurate against NMDA-induced retinal damage involves restoration of minerals and trace elements homeostasis

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Abstract
Glutamate-mediated excitotoxicity involving N-methyl-d-aspartate (NMDA) receptors has been recognized as a final common outcome in pathological conditions involving death of retinal ganglion cells (RGCs). Overstimulation of NMDA receptors results in influx of calcium (Ca) and sodium (Na) ions and efflux of potassium (K). NMDA receptors are blocked by magnesium (Mg). Such changes due to NMDA overstimulation are also associated with not only the altered levels of minerals but also that of trace elements and redox status. Both the decreased and elevated levels of trace elements such as iron (Fe), zinc (Zn), copper (Cu) affect NMDA receptor excitability and redox status. Manganese (Mn) and selenium (Se) are also part of antioxidant defense mechanisms in retina. Additionally endogenous substances such as taurine also affect NMDA receptor activity and retinal redox status. Therefore, the aim of this study was to evaluate the effect of Mg acetyltaurate (MgAT) on the retinal mineral and trace element concentration, oxidative stress, retinal morphology and retinal cell apoptosis in rats after-NMDA exposure. One group of Sprague Dawley rats received intravitreal injection of vehicle while 4 other groups similarly received NMDA (160nmolL⁻¹). Among the NMDA injected groups, 3 groups also received MgAT (320nmolL⁻¹) as pre-treatment, co-treatment or post-treatment. Seven days after intravitreal injection, rats were sacrificed, eyes were enucleated and retinae were isolated for estimation of mineral (Ca, Na, K, Mg) and trace element (Mn, Cu, Fe, Se, Zn) concentration using Inductively Coupled Plasma (DRC ICP-MS) techniques (NexION 300D), retinal oxidative stress using Elisa, retinal morphology using H&E staining and retinal cell apoptosis using terminal deoxynucleotidyl transferase dUTP nick-end labeling (TUNEL). Intravitreal NMDA injection resulted in increased concentration of Ca (4.6 times, p<0.0001), Mg (1.5 times, p<0.01), Na (3 times, p<0.0001) and K (2.3 times, p<0.0001) compared to vehicle injected group. This was accompanied with significant increase of Ca/Mg and Na/K ratios, 3 and 1.27 times respectively, compared to control group. The trace elements such as Cu, Fe and Zn also showed a significant increase amounting to 3.3 (p<0.001), 2.3 (p<0.0001) and 3 (p<0.0001) times respectively compared to control group. Se was increased...
by 60% (p<0.005). Pre-treatment with MgAT abolished effect of NMDA on minerals and trace elements more effectively than co- and post-treatment. Similar observations were made for retinal oxidative stress, retinal morphology and retinal cell apoptosis. In conclusion, current study demonstrated the protective effect of MgAT against NMDA-induced oxidative stress and retinal cell apoptosis. This effect of MgAT was associated with restoration of retinal concentrations of minerals and trace elements. Further studies are warranted to explore the precise molecular targets of MgAT. Nevertheless, MgAT seems a potential candidate in the management of diseases involving NMDA-induced excitotoxicity.

**Keywords:** Calcium (Ca), Copper (Cu), Excitotoxicity, Ganglion cell layer (GCL), Inductively coupled plasma-mass spectrometry (ICP-MS), Iron (Fe), Magnesium (Mg), Magnesium acetyltaurate (MgAT), Manganese (Mn), Minerals, N-methyl-d-aspartate (NMDA), Potassium (K), Retina, Selenium (Se), Sodium (Na), Trace elements, Zinc (Zn).
Recent advances in galactose-engineered nanocarriers for the site-specific delivery of siRNA and anticancer drugs

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Abstract
Galactosylated nanocarriers have recently emerged as viable and versatile tools to deliver drugs at an optimal rate specifically to their target tissues or cells, thus maximizing their therapeutic benefits while circumventing offtarget effects. The abundance of lectin receptors on cell surfaces makes the galactosylated carriers suitable for the targeted delivery of bioactives. Additionally, tethering of galactose (GAL) to various carriers, including micelles, liposomes, and nanoparticles (NPs), might also be appropriate for drug delivery. Here, we review recent advances in the development of galactosylated nanocarriers for active tumor targeting. We also provide a brief overview of the targeting mechanisms and cell receptor theory involved in the ligand–receptor-mediated delivery of drug carriers.

**Methotrexate and beta-carotene loaded-lipid polymer hybrid nanoparticles: a preclinical study for breast cancer**

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**Abstract**

**Aim:** This work was intended to investigate the targeting potential of fructose-tethered lipid-polymeric hybrid nanoparticles (F-BC-MTX-LPHNPs) co-loaded with beta carotene (BC) and methotrexate (MTX) in breast cancer therapeutics and find out the possible protective role of BC on MTX-induced toxicity.

**Materials & methods:** F-BC-MTX-LPHNPs were fabricated using self-assembled nano-precipitation technique. Fructose was conjugated on the surface of the particles. The in vitro cytotoxicity, sub-cellular localization and apoptotic activity of F-BC-MTX-LPHNPs were evaluated against MCF-7 breast cancer cells. The antitumor potential of F-BC-MTX-LPHNPs was further studied.

**Results & discussion:** Outcomes suggested that F-BC-MTX-LPHNPs induced the highest apoptosis index (0.89) against MCF-7 cells. Following 30 days of treatment, the residual tumor progression was assessed to be approximately 32%, in animals treated with F-BC-MTX-LPHNPs. F-BC-MTX-LPHNPs are competent to selectively convey the chemotherapeutic agent to the breast cancers. Beta carotene ameliorated MTX-induced hepatic and renal toxicity.

**Keywords:** beta-carotene, bioavailability, breast cancer, lipid polymer hybrid nanoparticles, methotrexate, toxicity.
Pathogenesis of *Plasmodium berghei* ANKA infection in the gerbil (*Meriones unguiculatus*) as an experimental model for severe malaria

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Abstract

**Background:** As the quest to eradicate malaria continues, there remains a need to gain further understanding of the disease, particularly with regard to pathogenesis. This is facilitated, apart from in vitro and clinical studies, mainly via in vivo mouse model studies. However, there are few studies that have used gerbils (*Meriones unguiculatus*) as animal models. Thus, this study is aimed at characterizing the effects of *Plasmodium berghei* ANKA (PbA) infection in gerbils, as well as the underlying pathogenesis.

**Methods:** Gerbils, 5-7 weeks old were infected by PbA via intraperitoneal injection of 1 x 10\(^6\) (0.2 mL) infected red blood cells. Parasitemia, weight gain/loss, hemoglobin concentration, red blood cell count and body temperature changes in both control and infected groups were monitored over a duration of 13 days. RNA was extracted from the brain, spleen and whole blood to assess the immune response to PbA infection. Organs including the brain, spleen, heart, liver, kidneys and lungs were removed aseptically for histopathology.

**Results:** Gerbils were susceptible to PbA infection, showing significant decreases in the hemoglobin concentration, RBC counts, body weights and body temperature, over the course of the infection. There were no neurological signs observed. Both proinflammatory (IFNg and TNF) and anti-inflammatory (IL-10) cytokines were significantly elevated. Splenomegaly and hepatomegaly were also observed. PbA parasitized RBCs were observed in the organs, using routine light microscopy and in situ hybridization.

**Conclusion:** Gerbils may serve as a good model for severe malaria to further understand its pathogenesis. Keywords: Gerbil, *Plasmodium berghei* ANKA, Severe Malaria, Pathogenesis, Cytokines, In situ hybridization.
Legumain targeting peptide conjugated fluorescent porous silicon nanoparticles for breast cancer imaging

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Abstract
Porous silicon (PSi) with a suite of most desirable biomaterial properties has attracted great attention as a multifunctional nanoplatform for bioimaging and drug delivery. Various surface functionalization treatments have been reported for PSi to use as an active tumor cell targeting nanovector. In this study, we investigated surface functionalization treatments using a peptide that is specific to the emerging biomarker legumain. The PSi nanoparticles were coated with dextran and subsequently two types of legumain targeting peptide, Y-shaped and linear chain, were conjugated to produce the functionalized PSi. The functionalized (ligand-conjugated) PSi materials were characterized for morphology, size, functional groups, and fluorescence response using electron and fluorescence microscopy and vibrational spectroscopy techniques. Fluorescence microscopy imaging with two excitation wavelengths (450 nm and 600 nm) suggests comparable fluorescence response of the conjugated PSi to “bare” PSi and the suitability of the PSi functionalized with peptide for bioimaging.

Keywords: Porous silicon, active targeting, legumain, bioimaging, nanomedicine.
A metabolic stability determination of Tetrahydrothiazolopyridine derivative a selective 11β-hydroxy steroid dehydrogenase type 1 (11β-hsd1) inhibitor

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Abstract
A potent tetrahydrothiazolopyridine derivative TR-018A that acts as an inhibitor of 11β-Hydroxysteroid dehydrogenase isoform 1 was investigated for its metabolic stability in mouse, rat and human liver microsomes. The study was carried out in two parts, one is to develop a method in high-performance liquid chromatography for TR-018A and the other is to investigate its metabolic stability in rat, human and mouse liver microsomes. The chromatograms and retention time for TR-018A were analyzed at different time points; control, 0, 5, 15, 30 and 60 minutes by using Betasil C18 column (5 μm particle size, 150mm X 4.6mm by Thermo Scientific.) at column temperature 40°C with an isocratic mobile phase containing acetonitrile and 0.2% formic acid of 0.7mL/min flow with 15 minutes run time, TR-018A chromatograms were detected and recorded at λ = 283nm with the injection volume of 20μL. Under the provided experimental conditions, it was observed that Tetrahydrothiazolopyridine compound TR-018A was stable in mouse, rat and human liver microsomes and stable up to ~80% at 30 min of incubation. This study shows that the compound is a metabolically stable and the results indicated that 11β-HSD1 inhibition by TR-018A may serve as a potential novel treatment for Type 2 diabetes and worth conducting further preclinical evaluations.

Keywords: Metabolic stability, 11β-HSD1 inhibitor, Liver microsomes, HPLC, tetrahydrothiazolopyridine.
Attitudes and readiness of students of healthcare professions towards interprofessional learning

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Abstract
Objectives: To evaluate the attitudes and readiness of students of healthcare professions towards interprofessional learning.

Methodology: A cross-sectional study design was used. Two different scales were used to measure the readiness for and perception of interprofessional learning; these were the ‘Readiness for Interprofessional Learning Scale’ and the ‘Interdisciplinary Education Perception Scale’. A convenience sampling method was employed. The sample was drawn from undergraduate students enrolled in years 1 to 5 of medical, dental, pharmacy and health sciences programme. Descriptive and inferential statistics were used to analyse the data.

Results: The overall response rate was 83%. The students mentioned that shared learning with other healthcare professional students will increase their ability to understand clinical problems. The students also mentioned that such shared learning will help them to communicate better with patients and other professionals. The students preferred to work with individuals from their own profession. Participants from medical, dental, pharmacy, and health sciences had a difference in opinion about ‘negative professional identity’, a domain of the Readiness for Interprofessional Learning Scale. Based on the different year of study of the students, ‘team work and collaboration’, ‘negative professional identity’ and ‘roles and responsibility’ were the Interdisciplinary Education Perception Scale domains where students had a difference in opinion.

Conclusions: Attitudes and readiness towards interprofessional learning showed significant differences among students of various healthcare professions; these differences also depended on the students’ year of study. Interprofessional learning should be incorporated in the curriculum of all healthcare professional programs, which may foster students to become competent healthcare providers and understand each profession’s role.
The charming tale of charm needles!

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Abstract
Charm needles or susuk are needle-shaped metallic objects inserted subcutaneously in different parts of the body. The practice of inserting susuk is, an indisputably cultural and superstitious traditional belief common in the south-east Asian region, especially to the people of Malaysia, Thailand, Singapore, Indonesia and Brunei. With increased use of diagnostic radiographs in dental or medical practice, the discovery of charm needles has become more frequent. We report one such case of charm needles inserted in oro-facial region which was discovered in routine dental radiograph, with emphasis on cultural and traditional belief.

Keywords: Susuk, charm needles, spiritual healing, traditional belief, panoramic radiograph.
Enhancing biopharmaceutical performance of an anticancer drug by long chain PUFA based self-nanoemulsifying lipidic nanomicellar system


Enhancing biopharmaceutical performance of an anticancer drug by long chain PUFA based self-nanoemulsifying lipidic nanomicellar system

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Abstract

The aim of this study was to develop polyunsaturated fatty acid (PUFA) long chain glyceride (LCG) enriched self-nanoemulsifying lipidic nanomicelles systems (SNELS) for augmenting lymphatic uptake and enhancing oral bioavailability of docetaxel and compare its biopharmaceutical performance with a medium-chain fatty acid glyceride (MCG) SNELS. Equilibrium solubility and pseudo ternary phase studies facilitated the selection of suitable LCG and MCG. The critical material attributes (CMAs) and critical process parameters (CPPs) were earmarked using Placket-Burman Design (PBD) and Fractional Factorial Design (FFD) for LCG- and MCG-SNELS respectively, and nano micelles were subsequently optimized using I- and D-optimal designs. Desirability function unearthed the optimized SNELS with $T_{emul}<5\text{min}$, $D_{nm}<100\text{nm}$, $\text{Rel}_{15\text{min}}>85\%$ and $\text{Perm}_{45\text{min}}>75\%$. The SNELS demonstrated efficient biocompatibility and energy dependent cellular uptake, reduced P-gp efflux and increased permeability using bi-directional Caco-2 model. Optimal PUFA enriched LCG-SNELS exhibited distinctly superior permeability and absorption parameters during ex vivo permeation, in situ single pass intestinal perfusion, lymphatic uptake and in vivo pharmacokinetic studies over MCG-SNELS.

Keywords: Bi-directional permeability, Docetaxel, Lymphatic uptake, Oral bioavailability, P-gp efflux, PUFA lipids, Quality by design.
Nanotechnology based approaches for anti-diabetic drugs delivery

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Abstract
Nanotechnology science has been diverged its application in several fields with the advantages to operate with nanometric range of objects. Emerging field of nanotechnology has been also being approached and applied in medical biology for improved efficacy and safety. Increased success in therapeutic field has focused several approaches in the treatment of the common metabolic disorder, diabetes. The development of nanocarriers for improved delivery of different oral hypoglycemic agents compared to conventional therapies includes nanoparticles (NPs), liposomes, dendrimer, niosomes and micelles, which produces great control over the increased blood glucose level and thus becoming an eye catching and most promising technology nowadays. Besides, embellishment of nanocarrirs with several ligands makes it more targeted delivery with the protection of entrapped hypoglycaemic agents against degradation, thereby optimizing prolonged blood glucose lowering effect. Thus, nanocarriers of hypoglycemic agents provide the aim towards improved diabetes management with minimized risk of acute and chronic complications. In this review, we provide an overview on distinctive features of each nano-based drug delivery system for diabetic treatment and current NPs applications in diabetes management.

Keywords: nanotechnology, insulin, diabetes, drug delivery.

**Dendrimer nanohybrid carrier systems: an expanding horizon for targeted drug and gene delivery**

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**Abstract**

Highly controllable dendritic structural design means dendrimers are a leading carrier in drug delivery applications. Dendrimer- and other nanocarrier-based hybrid systems are an emerging platform in the field of drug delivery. This review is a compilation of increasing reports of dendrimer interactions, such as dendrimer–liposome, dendrimer–carbonnanotube, among others, known as hybrid carriers. This should prompt entirely new research with promising results for these hybrid carriers. It is assumed that such emerging hybrid nanosystems – from combining two already-established drug delivery platforms – could lead the way for the development of newer delivery systems with multiple applicability for latent theranostic applications in the future.
Severe hemoptysis in a young man

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Abstract

A 34-year-old man comes to the respiratory outpatient department with complaints of large amounts of blood in the sputum since one day. He is a non-smoker and works as a clerk in an accounting office. There is no history of chest pain or breathlessness. He gives history of pulmonary tuberculosis 10 years ago for which he was given a 6 month course of anti-tuberculosis treatment to which he responded well. On examination, the patient’s vital parameters are normal. The trachea appears shifted to the right side. There is a hyper resonant note on percussion in the right supraclavicular and right infraclavicular regions anteriorly and bronchial breath sounds with increased vocal resonance are heard in the same area. The left lung examination is normal. A chest radiograph is urgently undertaken (Figure 1).

Keywords: Hemoptysis, Respiratory, Bronchoscopy, Ventilation.

**Polymeric nanocarriers: A new horizon for the effective management of breast cancer**

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**Abstract**

**Background**: Delivery of chemotherapeutic drugs for the diagnosis and treatment of cancer is becoming advanced day by day. However, the challenge of the effective delivery system still does exist. In various types of cancers, breast cancer is the most commonly diagnosed cancer among women. Breast cancer is a combination of different diseases. It cannot be considered as only one entity because there are many specific patient factors, which are involved in the development of this disease. Nanotechnology has opened a new area in the effective treatment of breast cancer due to the several benefits offered by this technology.

**Methods**: Polymeric nanocarriers are among one of the effective delivery systems, which has given promising results in the treatment of breast cancers. Nanocarriers does exert their anticancer effect either through active or passive targeting mode.

**Results**: The use of nanocarriers has been resolute about the adverse effects of chemotherapeutic drugs such as poor solubility and less penetrability in tumor cells.

**Conclusion**: The present review is focused on recent developments regarding polymeric nanocarriers, such as polymeric micelles, polymeric nanoparticles, dendrimers, liposomes, nanoshells, fullerenes, carbon nanotubes (CNT) and quantum dots, etc. for their recent advancements in breast cancer therapy.

**Keywords**: Nano-carriers, breast cancer, dendrimers, liposomes, nanoshells, polymeric nanoparticles, polymeric micelles, quantum dots.

**Unusual case of lamivudine-associated skin rashes in an HIV/AIDS patient: A case presentation**

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**Abstract**

In patients with human immunodeficiency virus (HIV) infection, lamivudine is used as a first-line drug for antiretroviral therapy. Lamivudine is relatively nontoxic in nature, and it can also be used during pregnancy. Herein, we describe a 43-year-old, HIV-positive female hospitalized with maculopapular, pruritic rash that appeared first on the extremities and gradually spread with systemic symptoms such as fever and myalgia after lamivudine therapy.

**Keywords:** Antiretroviral therapy, lamivudine, skin rash.
Dynamic fuzzy cognitive network approach for modelling and control of PEM fuel cell for power electric bicycle system

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Abstract
Modelling Proton Exchange Membrane Fuel Cell (PEMFC) is the fundamental step in designing efficient systems for achieving higher performance. Among the development of new energy technologies, modelling and optimization of energy processes with pollution reduction, sufficient efficiency and low emission are considered one of the most promising areas of study. Despite affecting factors in PEMFC functionality, providing a reliable model for PEMFC is the key of performance optimization challenge. In this paper, fuzzy cognitive map has been used for modelling PEMFC system that is directed to provide a dynamic cognitive map from the affecting factors of the system. Controlling and modification of the system performance in various conditions is more practical by correlations among the performance factors of the PEMFC derived from fuzzy cognitive maps. On the other hand, the information of fuzzy cognitive map modelling is applicable for modification of neural networks structure for providing more accurate results based on the extracted knowledge from the cognitive map and visualization of the system’s performance. Finally, a rule based fuzzy cognitive map has been used that can be implemented for decision-making to control the system. This rule-based Approach provides interpretability while enhancing the performance of the overall system.

Keywords: PEM fuel cell, Modelling, Fuzzy cognitive map, Rule-based FCM.
Emotional exhaustion is associated with work related stressors: A cross-sectional multicenter study in Malaysian public hospitals

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Abstract

Introduction: Emotional exhaustion is an important component of burnout. Burnout is common among doctors. It affects the physical and mental health of doctors, their performance and the quality of care they provide. This study aimed to investigate the level and factors associated with emotional exhaustion among doctors in pediatric practice in Malaysia.

Population and method: A self-administered questionnaire was used in this multicentre cross-sectional study. It included questions on the socio-demographics, work characteristics, Emotional Exhaustion, Perceived Stress Scale and sources of job stress. Descriptive, univariate and multivariate analysis were conducted using the SPSS software.

Results: A total of 197 doctors working in the Pediatric department in eight hospitals returned complete questionnaire. High and moderate emotional exhaustion was reported by 25.4% and 24.4% doctors, respectively. In bivariate analysis, 29 out of the 38 items of sources of stress showed significant association with emotional exhaustion (p <0.05). The significant predictors of emotional exhaustion in the multivariate analysis were: scoring higher on the Perceived Stress Score, dealing with patient’s psychosocial problems, disrespectful interactions with colleagues/subordinates, lack of appreciation from supervisors, lack of incentives and promotions, time pressures and deadlines to meet, and setting unrealistic goals of having them imposed on oneself (p <0.05). The most common source of stress was dealing with difficult parents (80.2%).

Conclusions: Emotional exhaustion is associated with sources of stress in the workplace but not with socio-demographic factors.

Keywords: burnout, professional, paediatrics, stress, workplace.
Khoo EJ, Schremmer RD, Diekema DS, Lantos JD. Ethics rounds: Ethical concerns when minors act as standardised patients. *Pediatrics*, 2017; 139: e20162795. (ISI IF: 5.705; CiteScore: 5.07; Tier: Q1).

**Ethics rounds: Ethical concerns when minors act as standardised patients**

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**Abstract**

When minors are asked to assist medical educators by acting as abstract standardized patients (SPs), there is a potential for the minors to be exploited. Minors deserve protection from exploitation. Such protection has been written into regulations governing medical research and into child labor laws. But there are no similar guidelines for minors’ work in medical education. This article addresses the question of whether there should be rules. Should minors be required to give their informed consent or assent? Are there certain practices that could cause harm for the children who become SPs? We present a controversial case and ask a number of experts to consider the ethical issues that arise when minors are asked to act as SPs in medical education.
Attitude, knowledge and ethical perception toward precision medicine among junior and senior medical students: Findings from one Malaysian medical school

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Abstract

Background: Medical schools are escalating changes to meet the need for doctors competent to work in the era of precision medicine. Information on the current level of awareness of precision medicine among medical students can help effect the necessary changes in the medical curriculum. A cross-sectional comparative study was done to assess the knowledge, attitude and perception toward the practice of precision medicine among junior and senior medical students in a medical school in Malaysia.

Materials and Method: A survey instrument measuring attitude toward precision medicine, perceived knowledge of genomic testing concepts, and perception toward ethical consideration related to precision medicine, was distributed to junior and senior medical students. Comparisons were made between senior and junior medical students.

Results: Only about one-third of the 356 respondents had heard of precision medicine although 92.7% expressed interest to learn more about precision medicine. Overall, junior and senior medical students had positive attitude toward the adoption of genome-guided prescribing and precision medicine but were uncomfortable with their knowledge of genomic testing concepts. Both junior and senior students were largely well grounded in their understanding of ethical issues related to precision medicine.

Conclusions: Knowledge of precision medicine was low among junior and senior medical students. Although the students supported the use of precision medicine, they did not feel adequately prepared to apply genomics to clinical practice. Their perceptions on ethical issues related to precision medicine were sound. Seniority did not appear to influence the perceptions of the students.

Keywords: precision medicine, personalised medicine, medical students, medical practice, medical education.
Concordance in the assessment of effectiveness of palliative care between patients and palliative care nurses in Malaysia: A study with the palliative care outcome scale

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Abstract

Context: The Palliative Care Outcome Scale (POS) is an easy-to-use assessment tool to evaluate the effectiveness of palliative care. There is no published literature on the use of POS as an assessment tool in Malaysia.

Aim: To define the concordance in the assessment of quality of life between patients with advanced cancers and their palliative care nurses using a Malay version of the POS.

Settings and Design: This study was conducted in the palliative care unit of the Hospital Tuanku Ja'afar Seremban, Malaysia, from February 2014 to June 2014.

Subjects and Methods: We adapted and validated the English version of the 3-day recall POS into Malay and used it to define the concordance in the assessment of quality of life between patients and palliative care nurses. Forty patients with advanced stage cancers and forty palliative care nurses completed the Malay POS questionnaire.

Statistical Analysis Used: The kappa statistical test was used to assess the agreement between patients and their palliative care nurses.

Results: Slight to fair concordance was found in all items, except for one item (family anxiety) where there was no agreement.

Conclusions: The Malay version of the POS was well accepted and reliable as an assessment tool for evaluation of the effectiveness of palliative care in Malaysia. Slight to fair concordance was shown between the patients and their palliative care nurses, suggesting the needs for more training of the nurses.

Keywords: Assessment tool, Malay, palliative care, Palliative Care Outcome Scale.

Missed opportunities for earlier HIV-testing in patients with HIV infection referred to a tertiary hospital, a cross-sectional study

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Abstract

Introduction: In Malaysia, the prevalence of missed opportunities for HIV-testing is unknown. Missed opportunities have been linked to late diagnosis of HIV and poorer outcome for patients. We describe missed opportunities for earlier HIV-testing in newly-HIV-diagnosed patients.

Methods: Cross sectional study. Adult patients diagnosed with HIV infection and had at least one medical encounter in a primary healthcare setting during three years prior to diagnosis were included. We collected data on sociodemographic characteristics, patient characteristics at diagnosis, HIV-related conditions and whether they were subjected to risk assessment and offered HIV testing during the three years prior to HIV diagnosis.

Results: 65 newly HIV-diagnosed patients (male: 92.3%; Malays: 52.4%; single: 66.7%; heterosexual: 41%; homosexual 24.6%; CD4 <350 at diagnosis: 63%). 93.8% were unaware of their HIV status at diagnosis. Up to 56.9% had presented with HIV-related conditions at a primary healthcare facility during the three years prior to diagnosis. Slightly more than half were had risk assessment done and only 33.8% were offered HIV-testing.

Conclusions: Missed opportunities for HIV-testing was unacceptably high with insufficient risk assessment and offering of HIV-testing. Risk assessment must be promoted and primary care physicians must be trained to recognize HIV-related conditions that will prompt them to offer HIV testing.

Keywords: Missed opportunities, HIV testing, risk assessment, primary care.
Age estimation from structural changes of teeth and buccal alveolar bone level

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Abstract
Forensic odontology plays a vital role in the identification and age estimation of unknown deceased individuals. The purpose of this study is to estimate the chronological age from Cone-Beam Computed Tomography (CBCT) images by measuring the buccal alveolar bone level (ABL) to the cemento-enamel junction and to investigate the possibility of employing the age-related structural changes of teeth as studied by Gustafson. In addition, this study will determine the forensic reliability of employing CBCT images as a technique for dental age estimation. A total of 284 CBCT images of Malays and Chinese patients (150 females and 134 males), aged from 20 years and above were selected, measured and stages of age-related changes were recorded using the i-CAT Vision software. Lower first premolars of both left and right side of the jaw were chosen and the characteristics described by Gustafson, namely attrition, secondary dentine formation and periodontal recession were evaluated. Linear regression analysis was performed for the buccal bone level and the R values obtained were 0.85 and 0.82 for left and right side respectively. Gustafson's characteristics were analysed using multiple regression analysis with chronological age as the dependent variable. The results of the analysis showed R values ranged from 0.44 to 0.62. Therefore it can be safely concluded that the buccal bone level highly correlated with the chronological age and is consequently the most suitable age-related characteristic for forensic age estimation.

Keywords: Cone-Beam Computed Tomography (CBCT), Age estimation, Gustafson's criteria, Attrition, Secondary dentin, Periodontal recession, Buccal bone level.
Anticancer mechanisms of Strobilanthes crispa Blume hexane extract on liver and breast cancer cell lines

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Abstract
Cancer is a major public health concern not only in developed countries, but also in developing countries. It is one of the leading causes of mortality worldwide. However, current treatments may cause severe side effects and harm. Therefore, recent research has been focused on identifying alternative therapeutic agents extracted from plant-based sources in order to develop novel treatment options for cancer. Strobilanthes crispa Blume is a plant native to countries including Madagascar and Indonesia. It has been used as an anti-diabetic, diuretic and laxative in traditional folk medicine. Furthermore, S. crispa has potential in treating cancer, as evidenced in previous studies. In the present study, the cytotoxic and apoptotic activities of S. crispa crude extracts were investigated in liver and breast cancer cell lines. Hexane, ethyl acetate, chloroform, methanol and water extracts prepared from the leaves, and stems of S. crispa were evaluated for their cytotoxicity on HepG-2 and MDA-MB-231 cells using an MTT assay. The anti-proliferative properties of stem hexane (SH) extract on both cell lines were analysed using cell doubling time determination and cell cycle analysis, while the apoptogenic properties was determined through the detection of caspase-8. Among the extracts tested, SH extract exhibited the lowest half maximal inhibitory concentrations in both the cell lines. The SH extract induced morphological changes in HepG-2 and MDA-MB-231 cells, and significantly delayed cell population doubling time. Furthermore, it altered cell cycle profile and significantly increased caspase-8 activity in HepG-2 cells, but not in MDA-MB-231 cells. In conclusion, the SH extract of S. crispa possesses potent anticancer properties and may be a suitable chemotherapeutic target.

Keywords: Strobilanthes crispa Blume, anticancer, apoptosis, breast cancer, liver cancer.
Abstract

Background: Provisional restorations are frequently needed for several days to weeks, demanding them to be well made and stable with distinctive functions and purposes. In aesthetically critical region, the provisional restoration must not only deliver an initial shade match, furthermore must preserve its aesthetic appearance over the service period. Noticeable colour change may compromise the suitability of provisional restorations.

Aim: This study aimed to determine the discolouration of poly (methyl methacrylate) (PMMA) and bis-acrylic based provisional crown and bridge auto-polymerizing resins when exposed to coffee, tea, orange and cranberry juice.

Materials and Methods: Four auto-polymerizing provisional crown and bridge resins, two methyl methacrylate and two bis-acrylic were used. Specimens were randomly divided into five groups (N=120, n=30) to be stored in artificial saliva, artificial saliva+tea, artificial saliva+coffee, artificial saliva+orange juice and artificial saliva+cranberry juice. Colour measurements were taken before immersion, after 1 week and 1 month of immersion with the Spectrophotometer. Data were analysed using analysis of variance (ANOVA), independent samples t-test, Scheffe’s post-hoc test, and paired t-test. A significance level of α = 0.05 was used for all statistical analyses.

Results: After the immersion period of 1 week and 1 month period, the post hoc analysis indicated that highest ΔE values were observed for Protemp II-artificial saliva + coffee as compared to other materials.

Conclusion: The degrees of discolouration increased with immersion time. Methyl methacrylate resins were more resistant to discolouration than bis-acrylic resins. After immersion for 1 month, artificial saliva + coffee solution resulted in unacceptable discolouration for all the tested materials.

Keywords: Crown and bridge resins, Discolouration, Duration, Provisional, Storage media.
Treatment of 3-prong anterior crossbite and unilateral lingual posterior crossbite malocclusion in an adolescent boy

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Abstract
R. V, a 16-year-old boy, presented with Class III end-on molar relationship on Class III skeletal base with below average mandibular plane angle and normal maxillomandibular differential. The upper canines were erupting, and late mixed dentition development was evident. Minimal spaces were present in both the arches. Normal transverse dimension of the dental arches was evident, but with some asymmetry in the mandibular arch. Left buccal segment was in lingual crossbite relationship, and the maxillary anterior teeth were characteristically locked in crossbite position with mandibular anterior teeth (3-prong crossbite). Treatment involved establishment of adequate curve of Wilson in the mandibular arch and mesialization of the maxillary buccal segment teeth using orthodontic miniscrews.

Keywords: Class III malocclusion, crossbites, miniscrew.
Interventions for managing taste disturbances

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Abstract

Background: The sense of taste is very much essential to the overall health of an individual. It is a necessary component to enjoy one's food, which in turn provides nutrition to an individual. Any disturbance in taste perception can hamper quality of life in such patients by influencing their appetite, body weight and psychological well-being. Taste disorders have been treated using different modalities of treatment and there is no consensus for the best intervention. Hence this Cochrane Review was undertaken. This is an update of the Cochrane Review first published in November 2014.

Objectives: To assess the effects of interventions for the management of patients with taste disturbances.

Search methods: Cochrane Oral Health's Information Specialist searched the following databases: Cochrane Oral Health’s Trials Register (to 4 July 2017); the Cochrane Central Register of Controlled Trials (CENTRAL; 2017 Issue 6) in the Cochrane Library (searched 4 July 2017); MEDLINE Ovid (1946 to 4 July 2017); Embase Ovid (1980 to 4 July 2017); CINAHL EBSCO (1937 to 4 July 2017); and AMED Ovid (1985 to 4 July 2017). The US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov) and the World Health Organization International Clinical Trials Registry Platform were searched for trials. Abstracts from scientific meetings and conferences were searched on 25 September 2017. No restrictions were placed on the language or date of publication when searching the electronic databases.

Selection criteria: We included all randomised controlled trials (RCTs) comparing any pharmacological agent with a control intervention or any nonpharmacological agent with a control intervention. We also included cross-over trials in the review.

Data collection and analysis: Two pairs of review authors independently, and in duplicate, assessed the quality of trials and extracted data. Wherever possible, we contacted trial authors for additional information. We collected adverse events information from the trials.

Main results: We included 10 trials (581 participants), nine of which we were able to include in the quantitative analyses (566 participants). We assessed three trials (30%) as having a low risk of bias, four trials (40%) at high risk of bias and three trials (30%) as having an unclear
risk of bias. We only included studies on taste disorders in this review that were either idiopathic, or resulting from zinc deficiency or chronic renal failure. Of these, nine trials with 544 people compared zinc supplements to placebo for patients with taste disorders. The participants in two trials were children and adolescents with respective mean ages of 10 and 11.2 years and the other seven trials had adult participants. Out of these nine, two trials assessed the patient-reported outcome for improvement in taste acuity using zinc supplements (risk ratio (RR) 1.40, 95% confidence interval (CI) 0.94 to 2.09; 119 participants, very low-quality evidence). We meta-analysed for taste acuity improvement using objective outcome (continuous data) in idiopathic and zinc-deficient taste disorder patients (standardised mean difference (SMD) 0.44, 95%CI 0.23 to 0.65; 366 participants, three trials, very low-quality evidence). We also analysed one cross-over trial separately using the first half of the results for taste detection (mean difference (MD) 2.50, 95% CI 0.93 to 4.07; 14 participants, very low-quality evidence), and taste recognition (MD3.00, 95%CI 0.66 to 5.34; 14 participants, very low-quality evidence). We metanalyzed taste acuity improvement using objective outcome (dichotomous data) in idiopathic and zinc-deficient taste disorder patients (RR 1.42, 95% 1.09 to 1.84; 292 participants, two trials, very low-quality evidence). Out of the nine trials using zinc supplementation, four reported adverse events like eczema, nausea, abdominal pain, diarrhoea, constipation, decrease in blood iron, increase in blood alkaline phosphatase, and minor increase in blood triglycerides. One trial tested taste discrimination using acupuncture (MD 2.80, 95% CI -1.18 to 6.78; 37 participants, very low-quality evidence). No adverse events were reported in the acupuncture trial. None of the included trials could be included in the meta-analysis for health-related quality of life in taste disorder patients.

**Authors’ conclusions:** We found very low-quality evidence that was insufficient to conclude on the role of zinc supplements to improve taste acuity reported by patients and very low-quality evidence that zinc supplements improve taste acuity in patients with zinc deficiency/idiopathic taste disorders. We did not find any evidence to conclude the role of zinc supplements for improving taste discrimination, or any evidence addressing health-related quality of life due to taste disorders. We found very low-quality evidence that is not sufficient to conclude on the role of acupuncture for improving taste discrimination in cases of idiopathic dysgeusia (distortion of taste) and hypogeusia (reduced ability to taste). We were unable to draw any conclusions regarding the superiority of zinc supplements or acupuncture as none of the trials compared these interventions.

**Novel 5-HT3 receptor antagonist QCM-4 attenuates depressive-like phenotype associated with obesity in high-fat-diet-fed mice**

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**Abstract**

**Rationale:** Depression associated with obesity remains an interesting area to study the biological mechanisms and novel therapeutic intervention.

**Objectives:** The present study investigates the effect of a novel 5-HT3 receptor antagonist 3-methoxy-N-p-tolylquinoxalin-2-carboxamide (QCM-4) on several pathogenic markers of depression associated with obesity such as plasma insulin resistance, hippocampal cyclic adenosine monophosphate (cAMP), brain-derived neurotrophic factor (BDNF), serotonin (5-HT) concentrations, hippocampal neuronal damage, and p53 protein expression in high-fat-diet (HFD)-fed mice.

**Methods:** Obesity was experimentally induced in mice by feeding with HFD for 14 weeks followed by administration of QCM-4 (1 and 2 mg/kg, p.o.)/standard escitalopram (ESC) (10 mg/kg, p.o.)/vehicle (10 ml/kg, p.o.) for 28 days. Behavioral assays such as sucrose preference test (SPT); forced swim test (FST); elevated plus maze (EPM); biochemical assays including oral glucose tolerance tests (OGTT), insulin, cAMP, BDNF, and 5-HT concentrations; and molecular assays mainly histology and immunohistochemistry (IHC) of p53 protein in the dentate gyrus (DG), CA1, and CA3 regions of hippocampus in HFD fed mice were performed.

**Results:** Chronic treatment with QCM-4 in HFD-fed mice reversed the behavioral alterations in SPT, FST, and EPM. QCM-4 showed poor sensitivity for plasma glucose, improved insulin sensitivity, increased hippocampal cAMP, BDNF, and 5-HT concentrations. In the hippocampal DG, CA1, and CA3 regions, QCM-4 treatment improved the neuronal morphology in the histopathology and inhibited p53 protein expression in IHC assay in HFD-fed mice.

**Conclusion:** QCM-4 attenuated the depressive-like phenotype in HFD-fed mice by improving behavioral, biochemical, and molecular alterations through serotonergic neuromodulation.

**Keywords:** BDNF, Depression, Obesity, Serotonin, p53.

**Does central vetting improve construct quality of one-best-answer items in medical school: An audit**

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**Abstract**

**Introduction:** Assessment is an integral aspect of teaching. One-best-answer (OBA) items, if properly constructed are able to drive learning. In-house OBA items are notoriously poorly-constructed. The role of a central vetting committee is to review test items and ensure that they adhere to expected standards. Hence, the objective of this audit is to determine whether central vetting has improved the construct quality of OBA items.

**Methods:** We audited the psychiatry end-of posting OBA items from before and after central vetting to compare the quality of the items before and after central vetting was instituted. Quality was evaluated on appropriateness of test content, items with higher cognition and items without flaws. A standard was not set for this first audit.

**Results:** Seventy-six of 181 psychiatry OBAs items retrieved from 2011 to August 2012 had undergone first level (department) vetting only and the remainder 105 (58.0%) had two levels of vetting; department and central vetting committee (CVC). Appropriateness of content increased from 92.1% to 98.1%. Items with higher order thinking doubled from 21.1% to 42.9%. Items with clinical scenario increased by 8.4% to 78.1%. Logical ordering of options however, remained around 50%. Two-level vetting markedly reduced problematic lead-in questions (67.1 to 13.3%), non-homogenous options (42.1 to 9.5%), vague and implausible options (39.5 to 6.7%), and spelling and grammar mistakes (19.7 to 5.7%).

**Conclusion:** Two-level vetting had improved the quality of OBAs and should be continued. This could be enhanced by training all Faculty on writing quality OBA items and careful selection and empowerment of CVC members. A re-audit is to be conducted after Faculty training.

**Keywords:** Assessment, Vetting, One-best-answer items, MCQ, Quality assurance.
Neuroprotective effect of magnesium acetyltaurate against NMDA-induced excitotoxicity in rat retina


Neuroprotective effect of magnesium acetyltaurate against NMDA-induced excitotoxicity in rat retina

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Abstract

Glutamate excitotoxicity plays a major role in the loss of retinal ganglion cells (RGCs) in glaucoma. The toxic effects of glutamate on RGCs are mediated by the overstimulation of N-methyl-D-aspartate (NMDA) receptors. Accordingly, NMDA receptor antagonists have been suggested to inhibit excitotoxicity in RGCs and delay the progression and visual loss in glaucoma patients. The purpose of the present study was to examine the potential neuroprotective effect of Mg acetyltaurate (MgAT) on RGC death induced by NMDA. MgAT was proposed mainly due to the combination of magnesium (Mg) and taurine which may provide neuroprotection by dual mechanisms of action, i.e., inhibition of NMDA receptors and antioxidant effects. Rats were divided into 5 groups and were given intravitreal injections. Group 1 (PBS group) was injected with vehicle; group 2 (NMDA group) was injected with NMDA while groups 3 (pre-), 4 (co-), and 5 (post-) treatments were injected with MgAT, 24 h before, in combination or 24 h after NMDA injection respectively. NMDA and MgAT were injected in PBS at doses 160 and 320 nmol, respectively. Seven days after intravitreal injection, the histological changes in the retina were evaluated using hematoxylin & eosin (H&E) staining. Optic nerves were dissected and stained in Toluidine blue for grading on morphological degenerative changes. The extent of apoptosis in retinal tissue was assessed by TUNEL assay and caspase-3 immunohistochemistry staining. The estimation of neurotrophic factor, oxidative stress, pro/anti-apoptotic factors and caspase-3 activity in retina was done using enzyme-linked immunosorbent assay (ELISA) technique. The retinal morphology showed reduced thickness of ganglion cell layer (GCL) and reduction in the number of retinal cells in GCL in NMDA group compared to the MgAT-treated groups. TUNEL and caspase-3 staining showed increased number of apoptotic cells in inner retina. The results were further corroborated by the estimation of neurotrophic factor, oxidative stress, pro/anti-apoptotic factors, and caspase-3 activity in retina. In conclusion, current study revealed that intravitreal MgAT prevents retinal and optic nerve damage induced by NMDA. Overall, our data demonstrated that the pretreatment with MgAT was more effective than co- and posttreatment. This protective effect of MgAT against NMDA-induced retinal cell apoptosis could be attributed to the reduction of retinal oxidative stress and activation of BDNF-related neuroprotective mechanisms.
**Keywords:** Excitotoxicity, Glaucoma, Magnesium acetyltaurate, NMDA, Neuroprotection, RGC apoptosis.
In vitro functional characterisation of cytochrome P450 (CYP) 2C19 allelic variants CYP2C19*23 and CYP2C19*24

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Abstract
Cytochrome P450 (CYP) 2C19 is essential for the metabolism of clinically used drugs including omeprazole, proguanil, and S-mephenytoin. This hepatic enzyme exhibits genetic polymorphism with inter-individual variability in catalytic activity. This study aimed to characterise the functional consequences of CYP2C19*23 (271 G>C, 991 A>G) and CYP2C19*24 (991 A>G, 1004 G>A) in vitro. Mutations in CYP2C19 cDNA were introduced by site-directed mutagenesis, and the CYP2C19 wild type (WT) as well as variants proteins were subsequently expressed using Escherichia coli cells. Catalytic activities of CYP2C19 WT and those of variants were determined by high performance liquid chromatography-based essay employing S-mephenytoin and omeprazole as probe substrates. Results showed that the level of S-mephenytoin 4′hydroxylation activity of CYP2C19*23 (V 111.5 ± 16.0 pmol/min/mg, K 158.3 ± 88.0 μM) protein relative to CYP2C19 WT (V 101.6 ± 12.4 pmol/min/mg, K 123.0 ± 19.2 μM) protein had no significant difference. In contrast, the K of CYP2C19*24 (270.1 ± 57.2 μM) increased significantly as compared to CYP2C19 WT (123.0 ± 19.2 μM) and V of CYP2C19*24 (23.6 ± 2.6 pmol/min/mg) protein was significantly lower than that of the WT protein (101.6 ± 12.4 pmol/min/mg). In vitro intrinsic clearance (CL = V /K for CYP2C19*23 protein was 85.4 % of that of CYP2C19 WT protein. The corresponding CL value for CYP2C19*24 protein reduced to 11.0 % of that of WT protein. These findings suggested that catalytic activity of CYP2C19 was not affected by the corresponding amino acid substitutions in CYP2C19*23 protein; and the reverse was true for CYP2C19*24 protein. When omeprazole was employed as the substrate, K of CYP2C19*23 (1911 ± 244.73 μM) was at least 100 times higher than that of CYP2C19 WT (18.37 ± 1.64 μM) and V of CYP2C19*23 (3.87 ± 0.74 pmol/min/mg) dropped to 13.4 % of the CYP2C19 WT (28.84 ± 0.61 pmol/min/mg) level. Derived from V /K, the CL value of CYP2C19 WT was 785 folds of CYP2C19*23. K and V values could not be determined for CYP2C19*24 due to its low catalytic activity towards omeprazole 5′hydroxylation. Therefore, both CYP2C19*23 and CYP2C19*24 showed marked reduced activities of metabolising omeprazole to 5hydroxyomeprazole. Hence, carriers of CYP2C19*23 and CYP2C19*24 allele are potentially poor metabolisers of CYP2C19 mediated substrates.

Keywords: CYP2C19, Polymorphism, HPLC, Functional characterisation.

**What role could community pharmacists in Malaysia play in diabetes self-management education and support? The views of individuals with type 2 diabetes**

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**Abstract**

**Objectives:** This study explored the experiences and views of individuals with type 2 diabetes mellitus (T2D) on their diabetes self-management and potential roles for community pharmacists in diabetes self-management education and support (DSME/S) in Malaysia.

**Methods:** A qualitative study, using semi-structured, face-to-face interviews, was conducted with patients with T2D attending a primary care health clinic in Kuala Lumpur, Malaysia. The interviews were audio-recorded, transcribed verbatim and analysed inductively.

**Key findings:** Fourteen participants with T2D were interviewed. Data were coded into five main themes: experience and perception of diabetes self-management, constraints of the current healthcare system, perception of the community pharmacist and community pharmacies, perceived roles for community pharmacists in diabetes care, and challenges in utilising community pharmacies to provide DSME/S. There were misconceptions about diabetes management that may be attributed to a lack of knowledge. Although participants described potential roles for community pharmacists in education, medication review and continuity of care, these roles were mostly non-clinically oriented. Participants were not confident about community pharmacists making recommendations and changes to the prescribed treatment regimens. While participants recognised the advantages of convenience of a community pharmacy-based diabetes care service, they raised concerns over the retail nature and the community pharmacy environment for providing such services.

**Conclusion:** This study highlighted the need to improve the care provision for people with T2D. Participants with T2D identified potential, but limited roles for community pharmacists in diabetes care. Participants expressed concerns that need to be addressed if effective diabetes care is to be provided from community pharmacies in Malaysia.

**Keywords:** community pharmacy, consumer attitudes, diabetes (clinical topics), patient attitudes (lay perspective), primary care (delivery of care).
Apoptosis gene network regulated by delta-tocotrienol in K562 chronic myeloid leukaemia cells

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Abstract
Palm oil is rich in various health-beneficial phytonutrients. The Vitamin E and the carotenoids make up a large portion of these phytonutrients. The tocotrienols are a relatively newer class of Vitamin E isoforms that are actively being researched for its various health promoting properties. In this study, the anti-cancer properties of the delta-tocotrienol (δ-T3) isoform were investigated on a leukemic cell line. A preliminary cytotoxicity assay was carried out to identify δ-T3’s potency in inducing cell death. Following this a real time-based gene array experiment was carried out to distinguish the apoptosis genes regulated by δ-T3 in the K562 leukemic cell line. Results show that treatment with δ-T3 significantly regulated the expression of several genes that promote apoptosis such as TP53, TP73, HRK, MCL1, CASP7, CASP8, DAPK1, PYCARD, FASLG and TNFRSF9. These findings suggest that palm δ-T3 can exert anti-cancer activities in chronic myeloid leukemic cells.

Keywords: Apoptosis, Cytotoxicity, Tocotrienol.

Understanding Giardia infections among rural communities using the one health approach

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Abstract

The epidemiology of giardiasis in rural villages in Peninsular Malaysia was examined in the context of the One Health triad that encompasses humans, animals and environment (i.e. river water). A cross-sectional study was carried out among five rural communities in Malaysia to determine the prevalence of *Giardia duodenalis* in humans, animals and river water. Fecal samples collected from humans and animals were examined by light microscopy. Water was sampled from the rivers adjacent to the target communities and investigated for the occurrence of Giardia cysts. The isolated cysts were further genotyped targeting the glutamate dehydrogenase and triosephosphate isomerase genes. The overall prevalence of *G. duodenalis* was 6.7% (18/269) and 4.7% (8/169) among humans and animals, respectively. Giardia cysts (mean concentration range: 0.10-5.97 cysts/L) were also found in adjacent rivers at four out of the five villages examined. At Kemensah and Kuala Pangsun, Giardia cysts were isolated from humans [rate: 3.7% each (of 54 each)], animals [rates: 6.3% (of 62) and 11.3% (of 16), respectively] and river water [average concentration of 9 samples each: 0.83±0.81 and 5.97±7.00, respectively]. For both villages at Pos Piah and Paya Lebar, 12.2% (of 98) and 6.1% (of 33) of collected human samples were infected, respectively whilst none of the collected animals samples in these villages were found to be positive. The river water samples of these two villages were also contaminated (average concentration: 0.20±0.35 (of 9) and 0.10±0.19 (of 3), respectively). In conclusion, Giardia cysts were simultaneously observed in the human-animal-environment (i.e., river water) interfaces in at least two of five studied communities highlighting a vital need to improve understanding on the interplay of transmission dynamics, the role of infected humans and animals in contaminating the water sources and the role of water as a vehicle of disease transmission in these communities. Indeed, this study illustrates the One Health approach which is to recognize that the optimal health of humans are interconnected with the well-being of animals and their environment.

Keywords: *Giardia duodenalis*, Human-animal-environment interfaces, Malaysia, One health approach.
Lee SY, Ng A, Singh MSJ, Liew YK, Gan SN, Koh RY. Physicochemical and antimicrobial properties of natural rubber latex films in the presence of vegetable oil microemulsions. *Journal of Applied Polymer Science*, 2017; 134: 1. [BP1–01/12(50)2015 [IG441]]. (ISI IF: 1.86; CiteScore: 1.74; Tier: Q2).

**Physicochemical and antimicrobial properties of natural rubber latex films in the presence of vegetable oil microemulsions**

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**Abstract**

A series of vegetable oil microemulsions are formulated and incorporated into NR latex to study the potent antimicrobial activity of vegetable oil-plasticized NR latex film against the adherent bacteria on the treated film. The particle size of latex incorporated with 2.50 phr of oil has attained up to 424 nm after incubated at 35±2°C for 24 h. The tensile stress of all NR latex films are relatively low, ranged 0.289 to 0.511 MPa. All emulsions are found compatible with NR and the low contact angles (<90°) corresponded to no oil blooming onto the surfaces of NR latex films. The crosslink densities are in good correlation with tensile strengths. The potent antimicrobial properties of the NR latex films are investigated from the viability assessment of the adherent tested *Escherichia coli* ATCC 25922 (*E. coli* ATCC 25922) and *Staphylococcus aureus* ATCC 25923 (*S. aureus* ATCC 25923). Results shows that NR latex film incorporated with palm kernel oil/soybean oil blend, NR-E(P/S57/3), has significantly killed the adherent *S. aureus* with 92.5% reduction but showed no significant log reduction in *E. coli*.

**Keywords:** antimicrobial, natural rubber latex film, vegetable oil microemulsion.
Perceived needs of patients undergoing coronary artery bypass graft surgery during perioperative period

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Abstract

Introduction: Perioperative care is nursing care provided by perioperative nurses to surgical patients during the perioperative period. Its role is important as patients especially those who had undergone coronary artery bypass graft (CABG) surgery encounter high levels of psychological and physical stress.

Objective: To determine the needs of CABG patients throughout the perioperative period and how well those needs were met.

Methods: This is a cross sectional descriptive survey. A total of 88 patients who had undergone coronary artery bypass graft were recruited through census sampling. The instrument which was adapted and used with permission for this study was “Survey of Patient Needs and Experiences during the Perioperative Period” questionnaire (Davis et al., 2014).

Results: The patients perceived the perioperative needs in the post-anaesthesia care unit area to be the most important (M = 2.89, SD = 0.06). Perioperative needs which were rated the highest for each of the four time periods were “Having information about the surgical procedure itself”, “Having your family member or significant other with you in the pre-surgical area complications”, “Being treated with respect and with dignity by hospital personnel” and “Having your family member or significant other visit you in the recovery room”. Overall, patients perceived their needs during perioperative period to be partly met (M = 2.73, SD = 0.07) with post-anaesthesia care unit area being rated the highest (M = 2.81, SD = 0.06).

Conclusion: The results of this study highlighted the perceived needs of patients undergoing coronary artery bypass graft surgery throughout their perioperative period. In order to improve the quality of perioperative care for patients, nurses need to take into consideration the important needs identified by the patients and address the items which were not meeting the needs of the patients.

Keywords: Coronary artery bypass graft, Intra-operative care, Operating theatre, Perioperative care, Pre-operative care, Post-anaesthesia care.
Preparation and optimization of palm-based lipid nanoparticles loaded with griseofulvin

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Abstract
Palm-based lipid nanoparticle formulation loaded with griseofulvin was prepared by solvent-free hot homogenization method. The griseofulvin loaded lipid nanoparticles were prepared via stages of optimisation, by altering the high pressure homogenisation (HPH) parameters, screening on palm-based lipids and Tween series surfactants and selection of lipid to surfactant ratios. A HPLC method has been validated for the drug loading capacity study. The optimum HPH parameter was determined to be 1500 bar with 5 cycles and among the palm-based lipid materials; Lipid C (triglycerides) was selected for the preparation of lipid nanoparticles. Tween 80 was chosen from the Tween series surfactants for its highest saturated solubility of griseofulvin at 53.1 ± 2.16 μg/mL. The optimum formulation of the griseofulvin loaded lipid nanoparticles demonstrated nano-range of particle size (179.8 nm) with intermediate distribution index (PDI) of 0.306, zeta potential of -27.9 mV and drug loading of 0.77%. The formulation was stable upon storage for 1 month at room temperature (25 °C) and 45 °C with consistent drug loading capacity.

Keywords: Lipid nanoparticles, Palm, Griseofulvin, Particle size, Drug loading, Stability, Zeta potential.
Liow JW, Khalaf ZF, Nur Amanina MA, Foong A. The experience of intimate relationships among homosexual men in Malaysia. *Sexuality and Culture*, 2017; 1-17. DOI: 10.1007/s12119-017-9442-x. [IMU Internal Grant - No. BPS I-1/13 (14) 2015]. (CiteScore: 0.79; Tier: Q1).

**The experience of intimate relationships among homosexual men in Malaysia**

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**Abstract**

Malaysia is relatively conservative regarding topics like sex, and, especially, research on homosexual relationships is scarce. The current study aims to understand the experience of intimate relationships among homosexual men in Malaysia using a phenomenological qualitative approach. A total of 12 participants of various ethnic backgrounds (between 21 and 35 years of age) were recruited through purposive and snowball sampling via the Malaysian-based LGBT-friendly Facebook group. Thematic analysis was applied for data analysis, and themes emerged through looking into the perception and practice of intimate relationships. The findings of the current study reflect that the hetero-normative perception of intimate relationships is common among the participants, and is compatible with the cultural norms. However, in terms of sexual practices, the findings show similarities with more liberal parts of the world, as open relationships and casual sex is common among homosexual men. Hence, open relationships are being adopted as a strategy to improve the survivability of the relationship instead of just to satisfy sexual needs. The findings highlight the lack of a frame of reference for homosexual relationships in Malaysia. The current study adds to the scarce research on homosexuality in this country, which could assist professional helpers to better understand the different dynamics and beliefs of relationships among homosexual men and the challenges they may face.

**Keywords:** Intimate relationship, Homosexual men, Sexual health.
Health-promoting effects of red palm oil: Evidence from animal and human studies

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Abstract

The fruit of the oil palm tree (Elaeis guineensis) is the source of antioxidant-rich red palm oil. Red palm oil is a rich source of phytonutrients such as tocotrienols, tocopherols, carotenoids, phytosterols, squalene, and coenzyme Q10, all of which exhibit nutritional properties and oxidative stability. Mutagenic, nutritional, and toxicological studies have shown that red palm oil contains highly bioavailable β-carotene and vitamin A and is reasonably stable to heat without any adverse effects. This review provides a comprehensive overview of the nutritional properties of red palm oil. The possible antiatherogenic, antihemorrhagic, antihypertensive, anticancer, and anti-infective properties of red palm oil are examined. Moreover, evidence supporting the potential effectiveness of red palm oil to overcome vitamin A deficiency in children and pregnant women, to improve ocular complications of vitamin A deficiency, to protect against ischemic heart disease, to promote normal reproduction in males and females, to aid in the management of diabetes, to ameliorate the adverse effects of chemotherapy, and to aid in managing hypobaric conditions is presented.
Genotypic and metabolic approaches towards the segregation of *Klebsiella pneumoniae* strains producing different antibiotic resistant enzymes

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Abstract

**Introduction:** Genotype and metabolomic variation are important for bacterial survival and adaptation to environmental changes.

**Objectives:** In this study, we compared the relationship among *Klebsiella pneumoniae* strains based on their genotypic and metabolic profiles. In addition, we also evaluated the association of the relationship with beta-lactamase production.

**Methods:** A total of 53 *K. pneumoniae* strains isolated in 2013–2014 from a tertiary teaching hospital in Malaysia were subjected to antimicrobial susceptibility testing (AST) via disk diffusion method and beta-lactamase production confirmation. The bacterial strains were also typed genotypically and metabolically via REP-PCR and ¹H-NMR spectroscopy respectively. The concordance of the matrices derived based on genotypic and metabolic characterization was measured based on Spearman’s rank correlation.

**Results:** Spearman’s correlation rank showed that there is a weak but significant negative correlation between the genetic fingerprints and metabolic profiles of *K. pneumoniae*. Specifically, *K. pneumoniae* strains were clustered into five major clusters based on REP-PCR where most of the carbapenem resistant *K. pneumoniae* (CRKP) strains made up the major cluster. In contrast, metabolic patterns of the three groups (i.e. CRKP, extended spectrum beta-lactamase producing *K. pneumoniae* (ESBL), susceptible) of *K. pneumoniae* were clearly differentiated on PLS-DA score plots derived from ¹H-NMR spectroscopy.

**Conclusion:** Overall, this study showed that metabolomic profiling using ¹H-NMR spectroscopy is able to discriminate *K. pneumoniae* strains based on their beta-lactamase production status.

**Keywords:** Carbapenem resistant, Extended spectrum beta-lactamase (ESBL), Nuclear magnetic resonance (NMR), Enterobacteriaceae, Metabolic profile, Repetitive extragenic palindromic PCR (REP-PCR).
The emergence of carbapenem resistant *Klebsiella pneumoniae* in Malaysia: Correlation between microbiological trends with host characteristics and clinical factors

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Abstract

**Background:** Carbapenem resistant Enterobacteriaceae is a growing concern worldwide including Malaysia. The emergence of this pathogen is worrying because carbapenem is one of the 'last-line' antibiotics. The main objective of this study was to determine the prevalence of genetic mechanisms and clinical risk factors of carbapenem resistant *Klebsiella pneumoniae* (*K. pneumoniae*) in Malaysia.

**Methods:** In this study, seventeen carbapenem resistant *K. pneumoniae* strains isolated from a tertiary teaching hospital in 2013 were studied. Minimal inhibitory concentration (MIC) of the bacterial strains was determined and genes associated with carbapenemases and extended-spectrum-beta-lactamases (ESBLs) were sequenced and compared with the closest representatives published in public domains. All strains were also sub-typed using pulsed-field gel electrophoresis (PFGE) and multilocus sequence typing (MLST). Statistical analyses were performed to determine the correlation between risk factors for acquiring carbapenem resistant *K. pneumoniae* and in-hospital mortality.

**Results:** The predominant carbapenemase was blaOXA-48, detected in 12 strains (70.59%). Other carbapenemases detected in this study were blaKPC-2, blaIMP-8, blaNMC-A and blaNDM-1. Nine different pulsotypes were identified and nine strains which were affiliated with ST101, the predominant sequence type had similar PFGE patterns (similarity index of 85%). Based on univariate statistical analysis, resistance to imipenem and usage of mechanical ventilation showed a statistically significant effect separately to in-hospital mortality.

**Conclusion:** The diverse genetic mechanisms harbored by these carbapenem resistant *K. pneumoniae* facilitates its spread and complicates its detection. Thus, correlation between microbiological trends with host characteristics and clinical factors will provide a better insight of rational treatment strategies and pathogen control.

**Keywords:** Carbapenem resistant *K. pneumoniae*, OXA-48, KPC-2, ST101, Enterobacteriaceae.
Prevalence and determinants of poor sleep quality among Myanmar migrant workers in Malaysia: A cross-sectional study

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Abstract

Background: Sleep quality is an important determinant of health; so much so that the socioeconomic and healthcare burden of poor sleep quality is alarming. In Malaysia, there is a shortage of sleep-quality studies conducted on Myanmar migrant workers, who comprise a significant proportion of the Malaysian workforce.

Aims: To identify the prevalence and determinants of poor sleep quality among Myanmar migrant workers in Malaysia.

Study Design: A cross-sectional study utilising systematic random sampling with replacement method.

Methodology: The study was conducted on 216 Myanmar migrant workers. A questionnaire was used to detect the socio-demographic information, health status, socio-economic information and lifestyle factors, and the Pittsburgh Sleep Quality Index (PSQI) was used to measure sleep quality.

Results: The prevalence of poor sleep quality was found in 62.5% of the study population. The factors significantly associated with poor sleep quality were body mass index (BMI) (OR = 0.462, 95% CI 0.225-0.950, P = 0.036), skill level (OR = 0.283, 95% CI 0.097-0.822, P = 0.020), shift work (OR = 3.393, 95% CI 1.456-7.908, P = 0.005), days worked per week (OR = 2.317, 95% CI 1.022-5.252, P = 0.044), working hours per day (OR = 2.305, 95% CI = 1.134-4.685, P= 0.021) and work-related physical tiredness (OR = 2.304, 95% CI = 1.186-4.476, P = 0.014).

Conclusions: The findings highlight the burden and determinants of poor sleep quality among Myanmar migrant workers in Malaysia. The prevalence of poor sleep quality was 62.5% of the study population. Six factors were associated with poor sleep quality in this population: having a lower BMI (Body mass index), being engaged in upper skill level jobs, being a shift worker, working 6 to 7 days a week and more than 8 hours per day and having to spend more than 30 minutes on a daily commute.

Keywords: Poor sleep quality, prevalence, determinants, Pittsburgh Sleep Quality Index (PSQI), Myanmar migrant workers, Malaysia.
In vitro and in vivo skin distribution of 5α-reductase inhibitors loaded into liquid crystalline nanoparticles

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Abstract

In this study, we developed positively charged liquid crystalline nanoparticles (LCN) coated with chitosan (CHI) to enhance the skin permeation and distribution of 5α-reductase inhibitors for the treatment of androgenetic alopecia. LCN and surface-modified LCN (CHI-LCN) were prepared by ultrasonication method, and their physicochemical properties were characterized. In vitro and in vivo skin permeation and retention were studied using porcine abdominal skin and mice skin using the Franz diffusion cell. Skin distribution and cellular uptake of LCN and CHI-LCN were also investigated. The particle size and surface charge were 244.9 ± 2.1 nm and -19.2 ± 1.1 mV, respectively, for LCNs and 300.0 ± 7.6 nm and 24.7 ± 2.4 mV, respectively, for CHI-LCN. The permeation of 5α-reductase inhibitors was significantly greater with CHI-LCN compared with LCN, whereas there was no significant difference observed in the skin distribution. In fluorescence studies, fluorescence intensity was higher for CHI-LCNs throughout the skin, whereas more intense fluorescence was seen only in the epidermis layer for LCN. CHI-LCN showed greater cellular uptake than LCN, resulting in internalization of 98.5 ± 1.9% of nanoparticles into human keratinocyte cells. In conclusion, surface modification of LCN with CHI is a promising strategy for increasing skin permeation of 5α-reductase inhibitors for topical delivery.

Keywords: 5α-reductase inhibitors, chitosan, liquid crystalline nanoparticles, skin distribution.
Anti-psychotic activity of aqueous root extract of *Hemidesmus indicus*: A time bound study in rats

Madhu A

Abstract

Aims and Background: Psychosis is a neurological disorder, which is usually defined as the “loss of contact with reality”. As medicine 'Hemidesmus indicus' holds a reputed place in all systems of medicine in India. It is given in the form of infusion, fine particles, or syrup. It is also a component of several medicinal preparations. The present research work is pertaining to find out an anti-psychotic activity of an aqueous root extract of *Hemidesmus indicus*- a time bound study in rats.

Methods: In the present study, the dried roots of *Hemidesmus indicus* were crushed to a coarse powder and extracted with water under reflux for 36 hours to obtain the aqueous extract of roots of *Hemidesmus indicus* (AERHI). The extract was reconstituted in 2% aqueous tragacanth just before use and administered orally at a dose of 100 mg/kg, 300 mg/kg and 500 mg/kg. In a single dose study, the parameters were assessed after oral administration of the single dose of the AERHI, whereas in a multiple dose study, the animals daily received the suitable oral dose of the AERHI for a period of 30 days. The parameters were assessed on the 15th and 30th day. The antipsychotic activity was screened using Apomorphine induced Stereotyped behavior in rats and Haloperidol induced catalepsy models were used. In Apomorphine induced Stereotyped behavior inhibition of the Stereotyped behavior was considered to be anti-psychotic activity and in Haloperidol induced catalepsy, we observed whether the AERHI potentiate or attenuate the catalepsy in rats.

Results: In this study, the extract of *Hemidesmus indicus* significantly inhibited the stereotyped behavior induced by apomorphine in rats and also potentiate the catalepsy induced by haloperidol, thereby showing its anti-psychotic activity.

Conclusion: All these observations imply that *Hemidesmus indicus* extract possesses anti-psychotic activity in experimental animals.

Keywords: Catalepsy, *Hemidesmus indicus*, anti-psychotic, aqueous root extract, catalepsy, stereotyped behaviour.
Cervical cancer prevention in Malaysia: Knowledge and attitude of undergraduate pharmacy students towards human papillomavirus infection, screening and vaccination in Malaysia

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Abstract
This study was conducted to evaluate knowledge of undergraduate pharmacy students about human papillomavirus infection and their attitude towards its prevention. A cross-sectional survey was conducted in 270 undergraduate pharmacy students using a validated questionnaire to assess knowledge about human papillomavirus infection and cervical cancer and their attitudes towards human papillomavirus vaccines. Eighty-one percent of the respondents knew that human papillomavirus is a cause of cervical cancer, and 87.8% knew that this infection is preventable. The gender of the respondents showed the strongest correlations with human papillomavirus knowledge. There were no significant correlations between the ethnic group of the respondents and their human papillomavirus-related knowledge. Higher perceptions of risk were associated with relationship status, and respondents who were in a relationship showed greater interest in vaccinating themselves; relationship status emerged as a unique predictor. The results indicated a moderately high level of knowledge and positive attitude towards human papillomavirus vaccination with few disagreements. The results of this study will help to develop and plan appropriate education campaigns for pharmacy students that aim to reduce human papillomavirus infection and, consequently, the incidence of and mortality caused by cervical cancer in Malaysia.

Keywords: Cervical cancer, Prevention, Pharmacy students, Vaccination, Malaysia.

**Predictors and factors associated with academic career decision-making among pharmacy students**

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**Abstract**

**Objective:** In this study, we investigated the predictors and factors associated with pharmacy students’ academic career as their future career option.

**Methods:** A sample of undergraduate pharmacy students studying in their final year was chosen as educational experiences may influence their career choice, and they would have gained more experiences than their juniors. A total of 135 students from one of the private universities in Malaysia participated in this study.

**Results:** `Interest in teaching` with standardised coefficient Beta value of 0.356 was the best predictor for the students accepting academia. `Minimal patient contact` with standardised coefficient Beta value of 0.573 was the best predictor for students rejecting academia.

**Discussion:** The students who were interested in teaching was minimal. Given the challenging nature of an academic career, there is a need to train more pharmacy academics.

**Keywords:** Pharmacy career, Pharmacy teaching, Malaysian academics, Malaysian students.

**Pharmacy students’ anxiety towards research during their undergraduate degree; How to reduce it?**

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**Abstract**

**Objective:** To measure pharmacy students' anxiety towards research and how academic support, academic effort, attitude and self-efficacy influence their research anxiety.

**Methods:** A cross-sectional study was conducted with undergraduate final year students of pharmacy using a convenient sampling method. A validated self-administered questionnaire was used.

**Results:** Response rate for this study was 85.9% (128 students from a population of 149). The participants agreed that they read literature to understand research, but did not attend research-related coursework. Most participants (91.4%) felt that they were under stress while doing research. Almost all participants (97.6%) felt that they were doing very badly during their data analysis or they may fail their research projects. The majority of participants agreed that help from the lecturers' and friends in research give emotional support for their research activities.

**Conclusion:** Academic support for pharmacy students, along with their additional academic effort will improve the students’ self-efficacy and reduce research anxiety.

In vitro inhibitory mechanisms and molecular docking of 1'-S-1'-acetoxychavicol acetate on human cytochrome P450 enzymes

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Abstract

Background: The compound, 1'-S-1'-acetoxychavicol acetate (ACA), isolated from the rhizomes of a Malaysian ethno-medicinal plant, *Alpinia conchigera* Griff. (Zingiberaceae), was previously shown to have potential in vivo antitumour activities. In the development of a new drug entity, potential interactions of the compound with the cytochrome P450 superfamily metabolizing enzymes need to be ascertain.

Purpose: The concomitant use of therapeutic drugs may cause potential drug-drug interactions by decreasing or increasing plasma levels of the administered drugs, leading to a suboptimal clinical efficacy or a higher risk of toxicity. Thus, evaluating the inhibitory potential of a new chemical entity, and to clarify the mechanism of inhibition and kinetics in the various CYP enzymes is an important step to predict drug-drug interactions.

Study design: This study was designed to assess the potential inhibitory effects of *Alpinia conchigera* Griff. rhizomes extract and its active constituent, ACA, on nine c-DNA expressed human cytochrome P450s (CYPs) enzymes using fluorescent CYP inhibition assay.

Methods/results: The half maximal inhibitory concentration (IC₅₀) of *Alpinia conchigera* Griff. rhizomes extract and ACA was determined for CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C19, CYP2D6, CYP2E1, CYP3A4 and CYP3A5. A. conchigera extract only moderately inhibits on CYP3A4 (IC₅₀ = 6.76 ± 1.88µg/ml) whereas ACA moderately inhibits the activities of CYP1A2 (IC₅₀ = 4.50 ± 0.10µM), CYP2D6 (IC₅₀ = 7.50 ± 0.17µM) and CYP3A4 (IC₅₀ = 9.50 ± 0.57µM) while other isoenzymes are weakly inhibited. In addition, mechanism-based inhibition studies reveal that CYP1A2 and CYP3A4 exhibited non-mechanism based inhibition whereas CYP2D6 showed mechanism-based inhibition. Lineweaver-Burk plots depict that ACA competitively inhibited both CYP1A2 and CYP3A4, with a Kᵢ values of 2.36 ± 0.03 µM and 5.55 ± 0.06µM, respectively, and mixed inhibition towards CYP2D6 with a Kᵢ value of 4.50 ± 0.08µM. Further, molecular docking studies show that ACA is bound to a few key amino acid residues in the active sites of CYP1A2 and CYP3A4, while one amino residue of CYP2D6 through predominantly Pi-Pi interactions.
Conclusion: Overall, ACA may demonstrate drug-drug interactions when co-administered with other therapeutic drugs that are metabolized by CYP1A2, CYP2D6 or CYP3A4 enzymes. Further in vivo studies, however, are needed to evaluate the clinical significance of these interactions.

Keywords: 1′-S-1′-acetoxychavicol acetate, Cytochrome P450, Drug interaction, Enzyme kinetics, Inhibition, Molecular docking.
Targeting legumain as a novel therapeutic strategy in cancers

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Abstract
Recent reports indicate that the tumor microenvironment plays a pivotal role in cancer development and progression, leading to a paradigm shift in the way cancer is studied and targeted. In contrast to traditional approaches, where only tumor cells are targeted for the treatment, an emerging approach is to develop therapeutics which target the tumor microenvironment while complementing or enhancing current treatments. Legumain (LGMN) is a newly identified target which is highly expressed in the tumor microenvironment and in tumor cells, and holds potential both as a biomarker and as a therapeutic target. This review will be the first to summarize the expression of LGMN in common cancers, as well as its roles in tumorigenesis and metastasis. This review also discusses the current developments and future prospects of targeting LGMN through the development of DNA vaccines, azo-peptides, small molecule inhibitors and LGMN activated prodrugs, highlighting the potential of LGMN as a target for cancer therapeutics.

Keywords: Legumain, cancer, tumor microenvironment, vaccine, azo-peptide, small molecules, prodrug.
Association of GSTM1, GSTT1 and GSTP1 Ile105Val polymorphisms with clinical response to imatinib mesylate treatment among Malaysian chronic myeloid leukaemia patients

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Abstract
The detoxifying activity of glutathione S-transferases (GST) enzymes not only protect cells from the adverse effects of xenobiotics, but also alters the effectiveness of drugs in cancer cells, resulting in toxicity or drug resistance. In this study, we aimed to evaluate the association of GSTM1, GSTT1 and GSTP1 Ile105Val polymorphisms with treatment response among Malaysian chronic myeloid leukaemia (CML) patients who everyday undergo 400 mg of imatinib mesylate (IM) therapy. Multiplex polymerase chain reaction (multiplex-PCR) was performed to detect GSTM1 and GSTT1 polymorphisms simultaneously and polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) analysis was conducted to detect the GSTP1 Ile195Val polymorphism. On evaluating the association of the variant genotype with treatment outcome, heterozygous variant (AG) and homozygous variant (GG) of GSTP1 Ile105Val showed significantly a higher risk for the development of resistance to IM with OR: 1.951 (95% CI: 1.186–3.209, P=0.009) and OR: 3.540 (95% CI: 1.305–9.606, P=0.013), respectively. Likewise, GSTT1 null genotype was also associated with a significantly higher risk for the development of resistance to IM with OR == 1.664 (95% CI: 1.011–2.739, P=0.045). Our results indicate the potential usefulness of GST polymorphism genotyping in predicting the IM treatment response among CML patients.

Keywords: GSTM1, GSTT1, GSTP1, chronic myeloid leukaemia, imatinib mesylate, single-nucleotide polymorphism.
Mani SD, Vengadasamy R, Hamdan SI. Japanese dichotomies and the individual identity in Haruki Murakami’s Colourless Tsukuru Tazaki. GEMA Online Journal of Language Studies, 2017; 17(1): 77-88. (CiteScore: 0.51; Tier: Q1).

Japanese dichotomies and the individual identity in Haruki Murakami’s Colourless Tsukuru Tazaki

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Abstract
Japanese indigenous terms such as uchi/soto (inside/outside) and omote/ura (front/back) are common dichotomies employed to understand the differences between expected behaviours associated with group dynamics such as promoting collective harmony rather than individual uniqueness. Haruki Murakami advocates that the Japanese need to move away from these dichotomies in order to embrace the true self and assert an individual voice. This dictum comes after he concluded his observations on the tragic 1995 sarin gas attacks in Japan and noted that individuals should be more assertive in forming their own voice rather than conforming to the collective voice. In his latest novel, Colourless Tsukuru Tazaki and His Years of Pilgrimage (2014), he presents a new narrative on individual negotiations with group consciousness. This article seeks to reveal the sense of individuality presented through the frame of the Japanese dichotomies and the psychological response of the main character, Tsukuru. The character will be analysed in relation to the group that he belongs to: in the context of the Japanese uchi (inside) or soto (outside) and within each context, representations of his omote (front) or ura (back) is examined. The findings expose that both uchi and soto are significant in developing individuality. More importantly, how the individual responds while in these contexts determines his ability to construct his identity. This reading suggests that Murakami fulfills his agenda by empowering the individual to explore various ways in being independent. The novel also indicates that the Japanese society is gradually manifesting a growing sense of individuality by departing from its codes of group consciousness.

Keywords: Group consciousness, Haruki Murakami, Identity, Japanese dichotomies, uchi/soto.
Can brain natriuretic peptides and osteoprotegerin serve as biochemical markers for the detection of aortic pathology in children and adolescents with turner syndrome?


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Abstract
Turner syndrome (TS) is a chromosomal disorder that affects 1:2,000 females. It results from either the complete or partial loss of the X chromosome as well as other aberrations. Clinical features of TS include short stature, delayed puberty, and congenital cardiac malformations. TS children also have an increased prevalence of cardiometabolic risk factors, which predisposes them to complications like coronary artery disease, cerebrovascular-related deaths, and aortic dissection. Early cardiac imaging, such as echocardiography and cardiac magnetic resonance imaging, are recommended to detect underlying aortic pathology. However, these modalities are limited by cost, accessibility, and are operator dependent. In view of these short-comings, alternative methods, like vascular biomarkers, are currently being explored. There are only a few studies that have examined the relationship between B-type natriuretic peptide (BNP), N-terminal pro BNP (NT pro-BNP), and osteoprotegerin (OPG) and aortic disease in TS, and thus the data are only in proof-of-concept stages. Further meticulous longitudinal studies are required before BNP, NT pro-BNP, and OPG are used as vascular biomarkers for the detection of aortic disease in childhood and adolescent TS.

Keywords: Turner syndrome, vasculopathy, B-type natriuretic peptide, n-terminal pro BnP, osteoprot.

**A comprehensive review on polyelectrolyte complexes**

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**Abstract**

Global research on polyelectrolytes at a fundamental and applied level is intensifying because the advantages of sustainability are being accepted in academia and industrial research settings. During recent decades, polyelectrolytes became one of the most attractive subjects of scientific research owing to their great potential in the areas of advanced technologies. Polyelectrolytes are a type of polymer that have multitudinous ionizable functional groups. Ionized polyelectrolytes in solution can form a complex with oppositely charged polyelectrolytes — a polyelectrolyte complex (PEC). The present article provides a comprehensive review on PECs and their classification, theory and characterization, as well as a critical analysis of the current research.

**More accurate oral cancer screening with fewer salivary biomarkers**

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**Abstract**

Signal detection and Bayesian inferential tools were applied to salivary biomarkers to improve screening accuracy and efficiency in detecting oral squamous cell carcinoma (OSCC). Potential cancer biomarkers are identified by significant differences in assay concentrations, receiver operating characteristic areas under the curve (AUCs), sensitivity, and specificity. However, the end goal is to report to individual patients their risk of having disease given positive or negative test results. Likelihood ratios (LRs) and Bayes factors (BFs) estimate evidential support and compile biomarker information to optimize screening accuracy. In total, 26 of 77 biomarkers were mentioned as having been tested at least twice in 137 studies and published in 16 summary papers through 2014. Studies represented 10 212 OSCC and 25 645 healthy patients. The measure of biomarker and panel information value was number of biomarkers needed to approximate 100% positive predictive value (PPV). As few as 5 biomarkers could achieve nearly 100% PPV for a disease prevalence of 0.2% when biomarkers were ordered from highest to lowest LR. When sequentially interpreting biomarker tests, high specificity was more important than test sensitivity in achieving rapid convergence toward a high PPV. Biomarkers ranked from highest to lowest LR were more informative and easier to interpret than AUC or Youden index. The proposed method should be applied to more recently published biomarker data to test its screening value.

**Keywords:** evidence synthesis, cancer, biomarkers, likelihood ratio, signal detection, Bayesian analysis.
Psychobiotics: A new approach for treating mental illness

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Abstract
Gut microbiomes may have a significant impact on mood and cognition, which is leading experts towards a new frontier in neuroscience. Studies have shown that increase in the amount of good bacteria in the gut can curb inflammation and cortisol level, reduces symptoms of depression and anxiety, lowers stress reactivity, improves memory and even lessens neuroticism and social anxiety. This shows that, probably the beneficial gut bacteria or probiotics function mechanistically as delivery vehicles for neuroactive compounds. Thus, a psychobiotic is a live organism, when ingested in adequate amounts, produces a health benefit in patients suffering from psychiatric illness. Study of these novel class of probiotics may open up the possibility of rearrangement of intestinal microbiota for effective management of various psychiatric disorders.

Keywords: Gut microbes, mental illness, psychobiotics.

**Rehabilitation of a patient with severely attrited dentition - A case report**

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**Abstract**

A patient with severely attrited dentition suffers from generalized sensitivity, mobility of teeth, compromised esthetics and decreased vertical dimension of occlusion which results in a dentition compromised in form, function and esthetics due to which the patient suffers from lack of confidence. The objectives of the treatment for such case should be preservation of the remaining tooth structure, restoration of optimum function, esthetics with least invasive procedures, cost effective treatment, and shorter treatment time.

**Keyword:** Rehabilitation, Severely attrited, Diagnostic wax up, Vertical dimension, Occlusal wear.

**Functional roles of receptor interacting protein kinase 1 in Alzheimer’s disease**

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International Medical University (IMU), Kuala Lumpur, Malaysia.

**Abstract**

Neurodegenerative diseases are a growing global issue. They tend to occur in the later stages of life and are primarily characterized by dementia, irritability, aggressiveness and poor cognitive function, among other manifestations. Pathologically, neurodegenerative diseases such as Alzheimer’s and Parkinson’s disease feature the progressive damage of neurons in the brain. Alzheimer’s disease in particular is the sixth leading cause of death in the US. Its aetiology involves impaired cell signaling pathways that are crucial for cell survival through the modulation of tumor necrosis factor-α activity via the actions of receptor interacting protein kinase (RIPK) 1. The study of RIPK1 involvement in Alzheimer’s disease had been ongoing for decades, and it was found to mediate two of the most common pathways implicated in the neuronal deaths seen in Alzheimer’s disease: apoptosis and necroptosis. To a certain extent, the involvement of autophagy was also observed in the progression of neuronal death. In this review, the general structure of RIPK1 and the various cell death pathways it regulates, as well as its significance in Alzheimer’s disease, are discussed.
Systematic review of metformin monotherapy and dual therapy with sodium glucose co-transporter 2 inhibitor (SGLT-2) in treatment of type 2 diabetes mellitus

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Abstract

Background: Type 2 Diabetes Mellitus (T2DM) is a chronic disorder and its treatment with only metformin often does not provide optimum glycemic control. Addition of sodium glucose co-transporter 2 inhibitor (SGLT2) will improve the glycemic control in patients on metformin alone. In this study, an attempt is made to investigate the combined therapy of SGLT-2 with metformin in managing T2DM in terms of lowering HbA1c and body weight and monotherapy using metformin alone in HbA1c and body weight reduction.

Objectives: To compare the clinical effectiveness of combined therapy using SGLT2 inhibitor and metformin with monotherapy using metformin alone in HbA1c and body weight reduction.

Method: A systematic review of the randomized controlled trials has been carried out and Cochrane risk of bias tool was used for the quality assessment. Patient, Intervention, Comparison and Outcomes (PICO) technique is used to select the relevant articles to meet the objective.

Results: The studies used in this article are multicenter, double-blinded randomized controlled trials on SGLT2 inhibitors with metformin, there were a total of 3897 participants, with a range of 182 to 1186 individual study size were included. Studies showed that combined therapy were more effective in HbA1c and body weight reduction as compared to monotherapy.

Conclusion: The combined therapy of SGLT2 inhibitor along with metformin is more effective in HbA1c reduction and weight reduction as compared to monotherapy using metformin alone. Among the three SGLT2 inhibitors such as dapagliflozin canagliflozin and empagliflozin do not differ much in the efficiency of weight reduction. However, Empagliflozin 25mg is effective in HbA1c reduction.

Keywords: Canagliflozin, Dapagliflozin, Empagliflozin, HbA1c, Metformin, SGLT2 inhibitors, Type 2 diabetes mellitus.
Musa I, Khaza’ai H, Mutalib MSA, Yusuf F, Sanusi J, Chang SK. Effects of oil palm tocotrienol rich fraction on the viability and morphology of astrocytes injured with glutamate. *Food Bioscience*, 2017; 20: 168–177. (ISI IF: 1.964; CiteScore: 2.43; Tier: Q1).

**Effects of oil palm tocotrienol rich fraction on the viability and morphology of astrocytes injured with glutamate**

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**Abstract**

Tocotrienol-rich fraction (TRF) is an extract of palm oil that consists of 25% α-tocopherol and 75% tocotrienols. TRF was shown to possess antioxidant, anti-inflammatory, anticancer, neuroprotective and cholesterol-lowering activities. Glutamate is the major mediator of excitatory signals in the mammalian central nervous system. Extreme amounts of glutamate in the extracellular spaces can lead to numerous neurodegenerative diseases. Hence, the efficacy of oil palm TRF and α-tocopherol in protecting astrocytes against glutamate-induced cell death was studied. Specifically, the effectiveness of pre- or post-treatment of TRF and α-tocopherol upon glutamate excitotoxicity was determined by evaluating cell viability and morphology of astrocytes. Cell viability was measured using MTT assay while cell morphology was monitored under fluorescent microscope using the acridine orange/propidium iodide (AO/PI) assay. Exposure to 230 mM glutamate significantly reduced cell viability to 50% in both the pre- and post-treatment studies; however, pre- and post-treatment with TRF and α-tocopherol attenuated the cytotoxic effect of glutamate. Compared to glutamate-injured astrocytes, pre-treatment with 100, 200 and 300 ng/ml TRF significantly improved cell viability following glutamate injury to 86.6%, 86.7% and 93.9%, respectively (p<0.05). On the contrary, high concentrations of α-tocopherol promote cell death. This study shows that TRF not only provide a better protection against glutamate toxicity (pretreatment), but was also able to reverse the lipid peroxidation resulting from glutamate insults (post-treatment). The present results demonstrate that TRF, but not α-tocopherol, protected the astrocytes against glutamate-induced cell death, indicating its neuro-protective potential.

**Keywords:** Glutamate, Tocotrienol rich fraction (TRF), Oil palm, α-tocopherol, Astrocytes, Viability.
Neuroendocrine carcinoma of the cervix: Review of classification and current developments in diagnosis and management

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Abstract

Neuroendocrine carcinoma of the female reproductive tract are a heterogeneous group of rare neoplasms posing both diagnostic and therapeutic challenges. The recent classification by WHO includes neuroendocrine carcinomas (NECs) and neuroendocrine tumours (NETs). NECs are the poorly differentiated small cell carcinoma (SCNEC) and large cell neuroendocrine carcinoma (LCNEC), while well-differentiated NETs include typical carcinoids (TC) and atypical carcinoids (AC). Majority of these tumours have an aggressive clinical course and published data is supportive of multi-modal therapeutic strategies. Etoposide/platinum based chemotherapy is commonly advocated. Histopathological categorisation and diagnosis are paramount to guide therapy. Well-differentiated carcinoid and atypical carcinoid tumours should be managed similar to gastroenteropancreatic neuroendocrine tumours. This review discusses the current classification, clinic-pathologic characteristics and advances in the diagnostic evaluation and the treatment options of neuroendocrine carcinoma of the cervix.

Keywords: High grade neuroendocrine tumours, well-differentiated neuroendocrine tumours, carcinoid tumours.
Factors associated with postobturation pain following single-visit nonsurgical root canal treatment: A systematic review

Nagendrababu V, Gutmann JL.

Abstract
Objective: Reducing the pain after root canal therapy is a key aspect in endodontic practice. The present systematic review aimed to identify the factors that influence postobturation pain (POP) in patients receiving single-visit nonsurgical root canal treatment.

Data Sources: A literature search was performed manually and in Pubmed (Medline) database to identify relevant articles. A data extraction form was constructed and data were collected from the identified articles.

Results: In total, 24 articles were identified for the systematic review, and factors associated with POP were tabulated.

Conclusion: Specific preoperative factors (old age, sex, molar teeth, mandibular teeth, presence of preoperative pain, and absence of periapical radiolucency) and procedures (administration of prophylactic drug, bupivicaine anesthetic agent, radiograph or apex locator working length determination methods, instrumentation, irrigating system, laser, cold lateral compaction obturation technique, reducing the occlusion, and postoperative drugs) were associated with POP.
Immediately modifiable risk factors attributable to colorectal cancer in Malaysia

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Abstract

Background: This study aimed to estimate potential reductions in case incidence of colorectal cancer attributable to the modifiable risk factors such as alcohol consumption, overweight and physical inactivity amongst the Malaysian population.

Methods: Gender specific population-attributable fractions (PAFs) for colorectal cancer in Malaysia were estimated for the three selected risk factors (physical inactivity, overweight, and alcohol consumptions). Exposure prevalence were sourced from a large-scale national representative survey. Risk estimates of the relationship between the exposure of interest and colorectal cancer were obtained from published meta-analyses. The overall PAF was then estimated, using the 2013 national cancer incidence data from the Malaysian Cancer Registry.

Results: Overall, the mean incidence rate for colorectal cancer in Malaysia from 2008 to 2013 was 21.3 per 100,000 population, with the mean age of 61.6 years (±12.7) and the majority were men (56.6%). Amongst 369 colorectal cancer cases in 2013, 40 cases (20 men, 20 women), 10 cases (9 men, 1 woman) or 20 cases (16 men,4 women) would be prevented, if they had done physical exercises, could reduce their body weight to normal level or avoided alcohol consumption, assuming that these factors are causally related to colorectal cancer. It was estimated that 66 (17.8%; 66/369) colorectal cancer cases (42 men, 24 women) who had all these three risk factors for the last 10 years would have been prevented, if they could control these three risk factors through effective preventive measures.

Conclusions: Findings suggest that approximately 18% of colorectal cancer cases in Malaysia would be prevented through appropriate preventive measures such as doing regular physical exercises, reducing their body weight to normal level and avoiding alcohol consumption, if these factors are causally related to colorectal cancer. Scaling-up nationwide public health campaigns tailored to increase physical activity, controlling body weight within normal limits and avoid alcohol intake are recommended. Future studies with other site-specific cancers and additional risk factors are needed.

Keywords: Colorectal cancer, Population-attributable fraction, Risk factors, Malaysia.

**Salivary glucose in monitoring glycaemia in patients with type 1 diabetes mellitus: A systematic review**

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Abstract

**Background:** Incidence of type 1 diabetes mellitus is increasing worldwide. Monitoring glycaemia is essential for control of diabetes mellitus. Conventional blood-based measurement of glucose requires venepuncture or needle prick, which is not free from pain and risk of infection. The non-invasiveness, ease and low-cost in collection made saliva an attractive alternative sample. The objective of this review was to systematically review the evidence on the relationship between salivary glucose level and blood glucose level in monitoring glycaemia in patients with type 1 diabetes mellitus.

**Methods:** We searched studies which evaluate salivary glucose levels and serum glycaemia in type 1 diabetes mellitus in electronic databases of MEDLINE, EMBASE, Ovid and Google Scholar. We selected the eligible studies, following the inclusion criteria set for this review. Due to heterogeneity of studies, we conducted qualitative synthesis of studies.

**Results:** Ten observational studies were included in this review, including a total of 321 cases and 323 controls with ages between 3 and 61 years and the majority were males (62%). Two studies were done exclusively on children below 17 years old. The significant difference between salivary glucose levels in type 1 diabetes mellitus and controls were reported in 6 studies with 8 data sets. Five studies with 7 datasets reported the correlation coefficient between salivary glucose and blood glucose in patients with diabetes.

**Conclusions:** Findings suggest that salivary glucose concentrations may be helpful in monitoring glycaemia in type 1 diabetes mellitus. However, the utility of using salivary glucose level to monitor glycaemia should be evaluated in future well designed, prospective studies with adequate number of participants with type 1 diabetes mellitus.

**Keywords:** Diabetes mellitus, Diagnosis, Glucose, Saliva, Systematic review.
Comparing antibiotic treatment for leptospirosis using network meta-analysis: A tutorial

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Abstract
Background: Network meta-analysis consists of simultaneous analysis of both direct comparisons of interventions within randomized controlled trials and indirect comparisons across trials based on a common comparator. In this paper, we aimed to characterise the conceptual understanding and the rationale for the use of network meta-analysis in assessing drug efficacy.

Methods: We selected randomized controlled trials, assessing efficacy of antibiotics for the treatment of leptospirosis as a case study. A pairwise meta-analysis was conducted using a random effect model, assuming that different studies assessed different but related treatment effects. The analysis was then extended to a network meta-analysis, which consists of direct and indirect evidence in a network of antibiotics trials, using a suite of multivariate meta-analysis routines of STATA (mvmeta command). We also assessed an assumption of ‘consistency’ that estimates of treatment effects from direct and indirect evidence are in agreement.

Results: Seven randomised controlled trials were identified for this analysis. These RCTs assessed the efficacy of antibiotics such as penicillin, doxycycline and cephalosporin for the treatment of human leptospirosis. These studies made comparisons between antibiotics (i.e. an antibiotic versus alternative antibiotic) in the primary study and a placebo, except for cephalosporin. These studies were sufficient to allow the creation of a network for the network meta-analysis; a closed loop in which three comparator antibiotics were connected to each other through a polygon. The comparison of penicillin versus the placebo has the largest contribution to the entire network (31.8%). The assessment of rank probabilities indicated that penicillin presented the greatest likelihood of improving efficacy among the evaluated antibiotics for treating leptospirosis.

Conclusions: Findings suggest that network meta-analysis, a meta-analysis comparing multiple treatments, is feasible and should be considered as better precision of effect estimates for decisions when several antibiotic options are available for the treatment of leptospirosis.
Anabolic steroids for treating pressure ulcers

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Abstract

Background: Pressure ulcers, also known as bed sores, pressure sores or decubitus ulcers develop as a result of a localised injury to the skin or underlying tissue, or both. The ulcers usually arise over a bony prominence, and are recognised as a common medical problem affecting people confined to a bed or wheelchair for long periods of time. Anabolic steroids are used as off-label drugs (drugs which are used without regulatory approval) and have been used as adjuvants to usual treatment with dressings, debridement, nutritional supplements, systemic antibiotics and antiseptics, which are considered to be supportive in healing of pressure ulcers. Anabolic steroids are considered because of their ability to stimulate protein synthesis and build muscle mass. Comprehensive evidence is required to facilitate decision making, regarding the benefits and harms of using anabolic steroids.

Objectives: To assess the effects of anabolic steroids for treating pressure ulcers.

Search methods: In March 2017 we searched the Cochrane Wounds Specialised Register; the Cochrane Central Register of Controlled Trials (CENTRAL); Ovid MEDLINE (including In-Process & Other Non-Indexed Citations); Ovid Embase and EBSCO CINAHL Plus. We also searched clinical trials registries for ongoing and unpublished studies, and scanned reference lists of relevant included studies as well as reviews, meta-analyses and health technology reports to identify additional studies. There were no restrictions with respect to language, date of publication or study setting.

Selection criteria: Published or unpublished randomised controlled trials (RCTs) comparing the effects of anabolic steroids with alternative treatments or different types of anabolic steroids in the treatment of pressure ulcers.

Data collection and analysis: Two review authors independently carried out study selection, data extraction and risk of bias assessment.

Main results: The review contains only one trial with a total of 212 participants, all with spinal cord injury and open pressure ulcers classed as stage III and IV. The participants were mainly male (98.2%, 106/108) with a mean age of 58.4 (standard deviation 10.4) years in the oxandrolone group and were all male (100%, 104/104) with a mean age of 57.3 (standard deviation 11.6) years in the placebo group. This trial compared oxandrolone (20 mg/day, administered orally) with a dose of placebo (an inactive substance consisting of 98% starch and 2% magnesium stearate) and reported data on complete healing of ulcers and adverse events.

There was very low-certainty evidence on the relative effect of oxandrolone on complete ulcer healing at the end of a 24-week treatment period (risk ratio RR) 0.81, 95% confidence interval (CI) 0.52 to 1.26) (downgraded twice for imprecision due to an extremely wide 95% CI, which spanned both benefit and harm, and once for indirectness, as the participants were mostly...
male spinal cord injury patients). Thus, we are uncertain whether oxandrolone improves or reduces the complete healing of pressure ulcers, as we assessed the certainty of the evidence as very low.

There was low-certainty evidence on the risk of non-serious adverse events reported in participants treated with oxandrolone compared with placebo (RR 3.85, 95% CI 1.12 to 13.26) (downgraded once for imprecision and once for indirectness, as the participants were mostly male spinal cord injury patients). Thus, the treatment with oxandrolone may increase the risk of non-serious adverse events reported in participants.

There was very low-certainty evidence on the risk of serious adverse events reported in participants treated with oxandrolone compared with placebo (RR 0.54, 95% CI 0.25 to 1.17) (downgraded twice for imprecision due to an extremely wide 95% CI, which spanned both benefit and harm, and once for indirectness, as the participants were mostly male spinal cord injury patients). Of the five serious adverse events reported in the oxandrolone-treated group, none were classed by the trial teams as being related to treatment. We are uncertain whether oxandrolone increases or decreases the risk of serious adverse events as we assessed the certainty of the evidence as very low.

Secondary outcomes such as pain, length of hospital stay, change in wound size or wound surface area, incidence of different type of infection, cost of treatment and quality of life were not reported in the included trial.

Overall the evidence in this study was of very low quality (downgraded for imprecision and indirectness). This trial stopped early when the futility analysis (interim analysis) in the opinion of the study authors showed that oxandrolone had no benefit over placebo for improving ulcer healing.

**Authors' conclusions:** There is no high quality evidence to support the use of anabolic steroids in treating pressure ulcers. Further well-designed, multicenter trials, at low risk of bias, are necessary to assess the effect of anabolic steroids on treating pressure ulcers, but careful consideration of the current trial and its early termination are required when planning future research.
Nalliah S, Gan PW, Premjit KMS, Naidu P, Lim V, Arshad ASAA. Comparison of efficacy and tolerability of pharmacological treatment for the overactive bladder in women: A network meta-analysis. *Australian Family Physician*, 2017; 46(3): 139-144. (ISI IF: 0.759; CiteScore: 0.55; Tier: Q3).

**Comparison of efficacy and tolerability of pharmacological treatment for the overactive bladder in women: A network meta-analysis**

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**Abstract**

**Background and objective:** Overactive bladder syndrome (OAB) is a common medical condition that causes significant distress and impact on the quality of life in women. Muscarinic receptor antagonists remain the mainstay of therapy, but they are limited by their efficacy and adverse effects. The objective of the article was to compare the clinical efficacy and tolerability of medications used to treat OAB in women through network meta-analysis.

**Methods:** Data from eligible studies of commonly prescribed pharmacological agents in the treatment of OAB in women were entered into NetMetaXL after a literature search using two online databases (PubMed and Cochrane). Studies between 31 July 2000 and 31 July 2015 were included in this study.

**Results:** Five quantitative studies were eligible for analysis. The most efficacious drug to treat OAB in women appears to be solifenacin 10 mg once daily (OD), followed by oxybutynin 3 mg three times a day. However, solifenacin 10 mg OD caused more adverse effects that the other treatments.

**Discussion:** Our results are similar to those of another systematic review. When considering efficacy, tolerability and cost, solifenacin 5 mg once daily is the drug of choice as it is more efficacious, albeit with more adverse effects, than other treatments. If solifenacin is unsuitable, oxybutynin 3 mg TDS is recommended.

**Development and validation of a RP-HPLC-UV method for simultaneous detection of caffeine and phenolphthalein in weight reducing supplements**

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**Abstract**

A sensitive, specific and reproducible liquid chromatography coupled to tandem mass spectrometric method was developed and validated for the estimation of ciprofloxacin, an extensively used second-generation quinolone antibiotics, in human plasma. A liquid-liquid extraction of ciprofloxacin and the internal standard, ofloxacin, has been approached from the biological matrix using chloroform. Chromatographic separation was achieved in positive ion modes, isocratically on a 3.5 μm C18 analytical column (75 mm×4.6 mm, i.d.) with 0.2% formic acid solution in water: methanol (10:90, v/v) as mobile phase, at a flow rate of 0.5 mL.min⁻¹. The MS/MS ion transitions were monitored as 332.0→231.3 for ciprofloxacin and 362.2→261.0 for IS. The method showed good linearity in the range of 0.01–5.00 μg.mL⁻¹ (r² >0.99) with a good precision (3.37–12.60%) and accuracy (87.25–114%). At the same time, ciprofloxacin was found to be stable during stability studies viz. benchtop, auto-sampler, freeze-thaw cycle and long-term. The developed and validated method was successfully applied to measure plasma ciprofloxacin concentrations in a single dose bioequivalence study.

**Keywords:** ciprofloxacin, LCMS/MS, bioequivalence study, human plasma, method validation.
Biofilms in endodontics - Current status and future directions

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Abstract
Microbiota are found in highly organized and complex entities, known as biofilms, the characteristics of which are fundamentally different from microbes in planktonic suspensions. Root canal infections are biofilm mediated. The complexity and variability of the root canal system, together with the multi-species nature of biofilms, make disinfection of this system extremely challenging. Microbial persistence appears to be the most important factor for failure of root canal treatment and this could further have an impact on pain and quality of life. Biofilm removal is accomplished by a chemo-mechanical process, using specific instruments and disinfecting chemicals in the form of irrigants and/or intracanal medicaments. Endodontic research has focused on the characterization of root canal biofilms and the clinical methods to disrupt the biofilms in addition to achieving microbial killing. In this narrative review, we discuss the role of microbial biofilms in endodontics and review the literature on the role of root canal disinfectants and disinfectant-activating methods on biofilm removal.

Keywords: bacteria, disinfection, extracellular polysaccharide, irrigation, root canal, review.
An evaluation of antimicrobial activity of different extracts of *Dillenia suffruticosa* stem bark

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Abstract
**Introduction:** The emergence of resistant microbes towards available antibiotics has spurred the search for new antimicrobial agents. *Dillenia* species have been widely used traditionally for a wide range of medicinal purposes by the indigenous people of Southeast Asia. Some *Dillenia* species have been shown to possess antimicrobial and antioxidant properties, however there are limited studies being carried out on *Dillenia suffruticosa*.

**Objectives:** To evaluate the antimicrobial activity of hexane, ethyl acetate, methanol and water extracts from the stem bark of *Dillenia suffruticosa* against twenty-one species of bacteria, fungi and yeasts.

**Methods:** The stem bark of *Dillenia suffruticosa* was extracted using Soxhlet apparatus. The dried extracts were diluted into seven different concentrations and impregnated onto filter paper discs. The antimicrobial activity of the extracts was evaluated through disc diffusion assay by measuring the zone of inhibition and proceeded with broth microdilution assay for the determination of minimum inhibitory concentration (MIC) using resazurin as a colorimetric indicator.

**Results:** In the disc diffusion test, all the four extracts were shown to have inhibitory effects on the growth of gram positive bacteria, with ethyl acetate and hexane extracts showing antimicrobial activity at lower concentrations as compared to methanol and water extracts. The only Gram-negative bacterium inhibited was *Proteus vulgaris* when tested against the methanol extract at 15 mg/mL. No antimicrobial activity was observed for all extracts against fungi and yeasts.

**Conclusion:** Hexane and ethyl acetate possess better antimicrobial properties compared to methanol and water extracts. Hence, phytochemical screening of the extracts needs to be carried out in order to determine the active compounds that are responsible for the antimicrobial activity of *Dillenia suffruticosa*.

**Keywords:** antimicrobial activity, *Dillenia suffruticosa*, disc diffusion assay, broth microdilution assay, resazurin.

*Clinacanthus nutans* hexane extracts induce apoptosis through a caspase-dependent pathway in human cancer cell lines

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Abstract

**Background:** *Clinacanthus nutans* (*C.nutans*) is a plant consumed as a cancer treatment in tropical Asia. Despite the availability of numerous anecdotal reports, evaluation of active anticancer effects has remained elusive. Therefore we here examined antiproliferative, reactive oxygen species (ROS)-inducing and apoptosis mechanisms of whole plant extracts in different cancer cell lines.

**Methods:** Antiproliferative actions of five solvent extracts (hexane, chloroform, ethyl acetate, methanol and water) of *C.nutans* were tested on non-small cell lung cancer (A549), nasopharyngeal cancer (CNE1) and liver cancer (HepG2) cells using MTT assay. The most potent anticancer extract was then assessed by flow cytometry to study cell cycle changes. Intracellular levels of ROS were quantified by DCFH-DA assay. Involvement of the caspase pathway in induction of apoptosis was assessed using caspase assay kits. GC-MS analysis was performed to identify phytoconstituents in the extracts.

**Results:** Hexane and chloroform extracts were antiproliferative against all three cell lines, while the ethyl acetate extract, at 300 μg/mL, was antiproliferative in the CNE1 but not A549 and HepG2 cases. Methanol and water extracts did not inhibit cancer cell proliferation. The most potent anticancer hexane extract was selected for further testing. It induced apoptosis in all three cell lines as shown by an increase in the percentage of cell in sub-G1 phase. Dose-dependent increase in ROS levels in all three cell lines indicated apoptosis to be possibly modulated by oxidative stress. At high concentrations (>100 μg/mL), hexane extracts upregulated caspases 8, 9 and 3/7 across all three cell lines. GC-MS analysis of the hexane extract revealed abundance of 31 compounds.

**Conclusion:** Among the five extracts of *C.nutans*, that with hexane extract demonstrated the highest antiproliferative activity against all three cancer cell lines tested. Action appeared to be via ion of intracellular ROS, and induction of apoptosis via intrinsic and extrinsic caspase pathways.

**Keywords:** *Clinacanthus nutans*, cancer, apoptosis, caspase, reactive oxygen species.
Ng WS, Lee CS, Chuah CH, Cheng SF. Preparation and modification of water-blown porous biodegradable polyurethane foams with palm oil-based polyester polyol. *Industrial Crops and Products*, 2017; 97: 65-78. [Collaborative project with UM, UM Research Grant(RG250-12AFR) and UM Postgraduate Research Fund (PG051-12AFR)]. (ISI IF: 3.449; CiteScore: 3.70; Tier: Q1).

**Preparation and modification of water-blown porous biodegradable polyurethane foams with palm oil-based polyester polyol**

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**Abstract**

Water-blown porous polyurethane foams were synthesized by one-shot foaming method. The effect of modification of polyurethane system with different content of newly synthesized palm oil-based polyester polyol (PPP) on the physical, chemical, mechanical and biodegradation properties of polyurethane foams were investigated. The resulting polyurethane foams were characterized by ATR-FTIR, Instron Universal Testing Machine, STA and SEM. The modification of polyurethane with PPP improved pore size and cell compactness, tensile strength, elastic modulus and elongation at break of the polyurethane foams. In terms of biodegradation properties, all the modified polyurethane foams were susceptible to enzymatic degradation. The degradation of modified polyurethane did not incur significant changes in pH of the medium used. After 7 days of enzymatic treatment, polyurethane prepared with 100 wt. % and 75 wt.% of PPP maintained 90% and 70% of the tensile strength, respectively. The current work demonstrated that the modification of water-blown porous polyurethane formulation with PPP allow improvement in physical and mechanical properties as well as tunable degradation rate with sustained mechanical strength, which may suitably use in soft and rigid tissue engineering applications.

**Keywords:** Palm oil-based, Polyester polyol, Polyurethane, Water-blown, Biodegradable polymers.
Health risk assessment of PM10 exposure among Malaysian adult population based on physical activity pattern

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Abstract

Introduction: Most health advisories related to outdoor physical activity during haze are general in nature. The advisories normally advise everyone to reduce or limit prolonged exertion or heavy exertion without mentioning the acceptable duration for performing outdoor physical activity causing difficulty for public to decide to stop or cancel a particular outdoor or sport event. The aim of this paper is to determine the acceptable duration for performing outdoor physical activity pattern during haze based on API level.

Methods: Health risk assessment approach that comprises of hazard identification, exposure assessment, dose-response, and risk characterization steps was used to determine the potential inhaled dose and risk associated with performing the physical activity during haze. We have considered many factors that include time spent for physical activity patterns for Malaysian adult, age and physical intensity-specific inhalation rate (m$^3$/min), and the indoor/outdoor ratio of PM$_{10}$. A hypothetical exposure scenario of PM$_{10}$ was created using the breakpoints of PM$_{10}$ concentration for the calculation of respective API levels during haze.

Results: The association between physical activity pattern, API level and risk quotient were presented in the form of risk radar diagram. Based on the 50th percentile inhalation rate, all prolonged exertion and heavy exertion should be avoided when API reach >201 (very unhealthy) and >175 (unhealthy) respectively. Below the said API, the duration for performing prolonged exertion and heavy exertion should be reduced according to the API level. When API reaches 140, high intensity physical activity should be limited to < 90 minutes. A football match which requires 90 minutes, should be postponed of cancelled if API > 140. Whereas, for the same API level, prolonged exertion (moderate intensity physical activity) should be limited to 4 hours.

Conclusions: Reducing the physical activity is an effective strategy to lower the dose of inhaled pollutants and reduce the health risk during poor air quality. Based on the assessment, taking into account the uncertainty of risk assessment methodology, we proposed all prolonged exertion should be avoided when API reach very unhealthy status (>201). Below the said API level, outdoor physical activity should be reduced according to the level of API respectively. The recommendation is not applicable for the sensitive groups. The computed risk radar provide a valuable guide for the public to organize or considering postponing an outdoor event during haze.

Keywords: Haze, PM10, Physical activity, risk assessment.
Delivering emergency and trauma care in Sri Lanka in 2017 – A decade of change and leadership by the Emergency Treatment Unit of Teaching Hospital Karapitiya


Abstract
Following the 2004 tsunami in Sri Lanka, the Health for the South Project was initiated by the Sri Lankan Ministry of Health, Teaching Hospital Karapitiya in Galle, and the Government of Victoria. With support from the Australian and Victorian Governments, the Alfred Hospital delivered the Capacity Building Component. The aim of the overall Project was to construct a fully equipped and staffed Emergency Trauma Centre; the aim of the Capacity Building Component was to increase the capacity of Teaching Hospital Karapitiya staff to deliver effective emergency and trauma care. The program included training in the systematic and team approach to trauma care plus triage, trauma quality improvement and disaster response. Following the formal completion of the Project, local medical and nursing champions have continued to improve the level of emergency and trauma care provided by Teaching Hospital Karapitiya; the facility is now a national and regional leader in the training and delivery of excellent emergency and trauma care.
The roles of cytochromes P450 in vascular biology and cardiovascular homeostasis

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Abstract
Cardiovascular disease and atherosclerosis are human health crises that remain the leading cause of death worldwide. The cytochromes P450 (CYPs) are key metabolizing enzymes of both xenobiotics and endobiotics. Many CYP enzymes have been identified in the heart, kidneys, endothelium, and smooth muscle of blood vessels. Furthermore, mounting evidence points to the role of endogenous CYP-dependent metabolites, such as epoxyeicosatrienoic acids (EETs), 20-hydroxyeicosatetraenoic acid (20-HETE), thromboxane A2 (TxA2) and prostacyclin (PGI2), in the maintenance of vascular physiology and cardiovascular homeostasis. The link between CYP genetic polymorphism and its pathological impact on cardiovascular disorders, such as hypertension and myocardial infarction, has been established in recent years. Therefore, there are numerous studies indicating the involvement of CYP in atherosclerotic and cardiovascular diseases. Currently, concentrating on treatment modalities that target the CYP pathways represents an attractive therapeutic strategy for the researchers in the field. While data are promising, further clinical investigation is necessary to understand fully the functional roles of the CYP enzymes in the regulation of vasculature and cardiovascular injuries in humans and to validate the safety of these potential therapeutic agents for use in patients.

Keywords: Arachidonic acid, cardiovascular homeostasis, cytochrome P450, eicosanoids, novel therapeutic agents, polymorphisms, prostanoids.
Single-walled carbon nanotubes (SWCNTs) inhibit heat shock protein 90 (HSP90) signaling in human lung fibroblasts and keratinocytes

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Abstract
Single-walled carbon nanotubes (SWCNTs) are carbon-based nanomaterials that possess immense industrial potential. Despite accumulating evidence that exposure to SWCNTs might be toxic to humans, our understanding of the mechanisms for cellular toxicity of SWCNTs remain limited. Here, we demonstrated that acute exposure of short (1-3 μm) and regular-length (5-30 μm) pristine, carboxylated or hydroxylated SWCNTs inhibited cell proliferation in human somatic and human stem cells in a cell type-dependent manner. The toxicity of regular-length pristine SWCNT was most evidenced in NP69 > CYT00086 > MCF-10A > MRC-5 > HaCaT > HEK-293T > HepG2. In contrast, the short pristine SWCNTs were relatively less toxic in most of the cells being tested, except for NP69 which is more sensitive to short pristine SWCNTs as compared to regular-length pristine SWCNTs. Interestingly, carboxylation and hydroxylation of regular-length SWCNTs, but not the short SWCNTs, significantly reduced the cytotoxicity. Exposure of SWCNTs also induced caspase 3 and 9 activities, mitochondrial membrane depolarization, and significant apoptosis and necrosis in MRC-5 embryonic lung fibroblasts. In contrast, SWCNTs inhibited the proliferation of HaCaT human keratinocytes without inducing cell death. Further analyses by gene expression profiling and Connectivity Map analysis showed that SWCNTs induced a gene expression signature characteristic of heat shock protein 90 (HSP90) inhibition in MRC-5 cells, suggesting that SWCNTs may inhibit the HSP90 signaling pathway. Indeed, exposure of MRC-5 cells to SWCNTs results in a dose-dependent decrease in HSP90 client proteins (AKT, CDK4 and BCL2) and a concomitant increase in HSP70 expression. In addition, SWCNTs also significantly inhibited HSP90-dependent protei refolding. Finally, we showed that ectopic expression of HSP90, but not HSP40 or HSP70, completely abrogated the cytotoxic effects of SWCNTs, suggesting that SWCNT-induced cellular toxicity is HSP90 dependent. In summary, our findings suggest that the toxic effects of SWCNTs are mediated through inhibition of HSP90 in human lung fibroblasts and keratinocytes.

Keywords: carbon nanotube, nanotoxicity, single-walled, nanomaterials, HSP90.
Honeycomb and necklace signs in liver abscesses secondary to melioidosis

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Abstract
Melioidosis is endemic in Southeast Asia and tropical Australia with varying clinical features from benign skin lesions to fatal septicaemia. Imaging plays an important role in evaluation of the melioid liver abscesses. A 45-year-old man with underlying diabetes presented with fever and lethargy for 2 weeks and abdominal pain for 2 days. His liver was enlarged on examination. Blood investigations revealed mild leucocytosis and raised liver enzymes. Ultrasound showed multiple multiloculated hypoechoic lesions throughout the liver and spleen. CT of abdomen confirmed that some liver lesions were made up of asymmetric locules of varying sizes (honeycomb sign), while others had hypodense centre with small symmetric peripheral locules in radial fashion (necklace sign). Blood culture was positive for Burkholderia pseudomallei. He was subsequently treated with ceftazidime for a month followed by oral trimethoprim–sulfamethoxazole for 3 months. Follow-up CT of abdomen a month after diagnosis and treatment showed resolving hepatic and splenic lesions.
Acute necrotizing encephalopathy of childhood: A review of two cases

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Abstract
Acute necrotising encephalopathy of childhood (ANEC) is an uncommon disease with characteristic clinical and imaging findings. We present two cases of ANEC secondary to Respiratory Syncytial Virus (RSV) and mycoplasma infections. An eight-month-old boy presented with features of gastroenteritis but soon developed multiple episodes of seizures. Blood and CSF cultures were negative but nasopharyngeal aspirate immunofluorescence was positive for RSV. A nine-year-old girl presented with abnormal behaviour following two days of prodromal symptoms. Her serological markers implicated mycoplasma (IgM titre 1: 640). CT brain of both patients showed bilateral symmetrical thalamic hypodensities, while MRI revealed more extensive white matter involvements.

Keywords: Gait disorders, gastroenteritis, mycoplasma infections, Respiratory Syncytial Viruses, seizures.

Chitosan-propolis nanoparticle formulation demonstrates anti-bacterial activity against Enterococcus faecalis biofilms

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Abstract
Propolis obtained from bee hives is a natural substance with antimicrobial properties. It is limited by its insolubility in aqueous solutions; hence ethanol and ethyl acetate extracts of Malaysian propolis were prepared. Both the extracts displayed antimicrobial and anti-biofilm properties against Enterococcus faecalis, a common bacterium associated with hospital-acquired infections. High performance liquid chromatography (HPLC) analysis of propolis revealed the presence of flavonoids like kaempferol and pinocembrin. This study investigated the role of propolis developed into nanoparticles with chitosan for its antimicrobial and anti-biofilm properties against E. faecalis. Bacteria that grow in a slimy layer of biofilm are resistant to penetration by antibacterial agents. The use of nanoparticles in medicine has received attention recently due to better bioavailability, enhanced penetrative capacity and improved efficacy. A chitosan-propolis nanoformulation was chosen based on ideal physicochemical properties such as particle size, zeta potential, polydispersity index, encapsulation efficiency and the rate of release of the active ingredients. This formulation inhibited E. faecalis biofilm formation and reduced the number of bacteria in the biofilm by ~90% at 200 μg/ml concentration. When tested on pre-formed biofilms, the formulation reduced bacterial number in the biofilm by ~40% and ~75% at 200 and 300 μg/ml, respectively. The formulation not only reduced bacterial numbers, but also physically disrupted the biofilm structure as observed by scanning electron microscopy. Treatment of biofilms with chitosan-propolis nanoparticles altered the expression of biofilm-associated genes in E. faecalis. The results of this study revealed that chitosan-propolis nanoformulation can be deemed as a potential anti-biofilm agent in resisting infections involving biofilm formation like chronic wounds and surgical site infections.
Abstract

Aims: There is a growing number of institutionalized elderly in Malaysia. This group of elderly are commonly not included in population based surveys, thus little is known about their health and well-being. This study aims to determine the self-rated health of the elderly living in institutions and the associated factors.

Methodology: This cross-sectional study was conducted in 2014, in eight elderly institutions in Kuala Lumpur. The institutions were selected randomly, and the participants were selected through stratified proportionate sampling. A total of 203 residents participated in this study. Chi-square test was used for univariate analysis and binary logistic regression was used for multivariate analysis. P value less than 0.05 were considered statistically significant.

Results: The prevalence of poor self-rated health was 39.9%. Factors significantly associated with self-rated health included educational level (OR=2.1, 95%CI=1.18-3.74), physical activity (OR=0.4, 95%CI=0.22-0.81) outdoor leisure activity (OR=0.4, 95%CI= 0.21-0.82), visual impairment (OR=1.9, 95%CI= 1.06-3.52), chronic pain (OR= 2.4, 95%CI=1.35-4.27), diabetes (OR=1.9, 95%CI=1.03-3.49) heart disease (OR=4.2, 95%CI=1.25-13.74), renal failure (OR=11.5, 95%CI=1.38-94.89), fall (OR=2.9, 95%CI= 1.28-6.48) hospitalization (OR=4.9, 95%CI= 2.43-9.86) comorbidities (OR=3.2, 95%CI=1.30-761), and satisfaction with access to healthcare (OR=0.3 95%CI= 0.17-0.79).

Conclusion: This study revealed a high prevalence of poor self-rated health among residents in these institutions. Factors significantly associated with self-rated health were mostly co-morbidities. There is need for interventions targeted at improving healthcare services and leisure activities for residents of these institutions.

Keywords: Elderly, Kuala Lumpur, self-rated health, institutionalized, Malaysia.
The correlation of *acanthamoeba* from the ventilation system with other environmental parameters in commercial buildings as possible indicator for indoor air quality

Ooi SS, Mak JW, Chen DK, Ambu S. The correlation of *acanthamoeba* from the ventilation system with other environmental parameters in commercial buildings as possible indicator for indoor air quality. *Industrial Health*, 2017; 55(1); 35-45. (ISI IF: 1.168; CiteScore: 1.14; Tier: Q2).

Abstract
The free-living protozoan *Acanthamoeba* is an opportunistic pathogen that is ubiquitous in our environment. However, its role in affecting indoor air quality and ill-health of indoor occupants is relatively unknown. The present study investigated the presence of *Acanthamoeba* from the ventilation system and its correlation with other indoor air quality parameters, used in the industry code of practice and its potential as an indicator for indoor air quality. Indoor air quality assessments were carried out in nine commercial buildings with approval from the building management, and the parameters assessed were as recommended by the Department of Occupational Safety and Health. The presence of *Acanthamoeba* was determined through dust swabs from the ventilation system and indoor furniture. Logistic regression was performed to study the correlation between assessed parameters and occupants' complaints. A total of 107 sampling points were assessed and 40.2% of the supplying air diffuser and blowing fan and 15% of the furniture were positive for cysts. There was a significant correlation between *Acanthamoeba* detected from the ventilation system with ambient total fungus count (r=0.327; p=0.01) and respirable particulates (r=0.276; p=0.01). Occupants' sick building syndrome experience also correlated with the presence of *Acanthamoeba* in the ventilation system (r=0.361; p=0.01) and those detected on the furniture (r=0.290; p=0.01). Logistic regression showed that there was a five-fold probability of sick building syndrome among occupants when *Acanthamoeba* was detected in the ventilation system.
Microwaved bacterial cellulose-based hydrogel microparticles for the healing of partial thickness burn wounds

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Abstract
Burn wound management is a complex process because the damage may extend as far as the dermis which has an acknowledged slow rate of regeneration. This study investigates the feasibility of using hydrogel microparticles composed of bacterial cellulose and polyacrylamide as a dressing material for coverage of partial-thickness burn wounds. The microparticulate carrier structure and surface morphology were investigated by Fourier transform infrared, X-ray diffraction, elemental analysis, and scanning electron microscopy. The cytotoxicity profile of the microparticles showed cytocompatibility with L929 cells. Dermal irritation test demonstrated that the hydrogel was non-irritant to the skin and had a significant effect on wound contraction compared to the untreated group. Moreover, histological examination of in vivo burn healing samples revealed that the hydrogel treatment enhanced epithelialization and accelerated fibroblast proliferation with wound repair and intact skin achieved by the end of the study. Both the in vitro and in vivo results proved the biocompatibility and efficacy of hydrogel microparticles as a wound dressing material.

Keywords: Hydrogel microparticles, Bacterial cellulose, Cytotoxicity, Partial-thickness burn wound, Microwave irradiation.
Comparative evaluation of indigenous ELISAs for detection of anti-cysticercus IgG antibodies in serum from clinically and radiologically suspected cases of neurocysticercosis

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Abstract

Neurocysticercosis (NCC) is an important but neglected tropical infectious disease, which is recently recognized as a global problem due to its potentiality for human-to-human transmission beyond tropics. The laboratory diagnosis of NCC is considered useful to confirm clinical and radiological diagnosis. However there is a lack of indigenous diagnostic method particularly in the tropical developing countries. Present study aimed to develop and evaluate indigenously developed anti-cysticercus IgG-ELISAs for possible diagnosis of NCC among patients presenting with seizures. Three indigenous antibody detection assays were developed employing three different antigenic preparations from \textit{T. solium} metacestode larvae (viz., TsM-CF, TsM-CW and TsM-PS). The overall test results showed varying levels of IgG titers in response to the three antigenic preparations as compared with the standard commercially procured antibody-ELISA. Total soluble protein extract of protoscoleces or TsM-PS-Ag employed in the indigenously developed IgG ELISA is recommended to be used as a routine screening test for a confirmatory diagnosis of NCC and other forms of cysticercosis in humans.
Correlation of salivary statherin and calcium levels with dental calculus formation: A preliminary study

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Abstract

Background: Salivary constituents have a wide range of functions including oral calcium homeostasis. Salivary proteins such as statherin inhibit crystal growth of calcium phosphate in supersaturated solutions and interact with several oral bacteria to adsorb on hydroxyapatite. Concurrently, saliva, which is supersaturated with respect to calcium phosphates, is the driving force for plaque mineralization and formation of calculus. Thus, the aim of the present study was to estimate and correlate salivary statherin and calcium concentration to the dental calculus formation.

Methods: A cross-sectional study was conducted to assess the relationship between salivary statherin, calcium, and dental calculus among 70 subjects, aged 20–55 years. Subjects were divided into 3 groups based on the calculus scores as interpreted by Calculus Index which was followed by collection of whole saliva using Super-SAL™. Salivary calcium levels were assessed by calorimetric method using Calcium Assay kit (Cayman Chemical, Michigan, USA) and statherin levels by using ELISA Kit (Cusabio Biotech).

Results: Statherin levels showed a weak negative correlation with the calcium levels and with calculus formation. The mean salivary statherin and calcium concentration were found to be 0.96 μg/ml and 3.87mg/ml, respectively. Salivary statherin levels differed significantly among the three groups (p < 0.05).

Conclusions: Our preliminary data indicates that statherin could possibly play a role in the formation of dental calculus.
Gas chromatography and mass spectroscopy analysis of bioactive components on the leaf extract of *Terminalia coriacea*: A potential folklore medicinal plant

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**Abstract**

**Aim:** This study aimed to investigate the bioactive constituents from methanolic extract of *Terminalia coriacea* leaves using gas chromatography and mass spectroscopy (GC-MS).

**Materials and Methods:** The methanolic extract obtained was subjected to GC-MS for the determination of bioactive volatile compounds. GC-MS analysis was carried out using 6890 GC with 5973 I MSD column.

**Results and Discussion:** The GC-MS analysis of the methanolic extract revealed the presence of 14 bioactive compounds with valuable biological activities. The major chemical constituents are 1H-inden-1-one,2,3-dihydro-3,3,5,6,- tetramethyl; levoglucosan; neophytadiene; phytol; hexadecanoic acid; n-hexadecanoic acid; stigmasterol; β-sitosterol; raffinose; 1,2-benzenedi carboxylic acid; undecanoic acid; (2 propyl-1,3-dioxolan-2-yl) acetic acid; 2,2 dimethyl propane, and octadecatrienoic acid.

**Conclusion:** The presence of various bioactive compounds in *T. coriacea* proved the pharmaceutical importance. It can be concluded that the plant investigation has opened up a new perspective in pharmaceutical research, and plants can be used for the development of potential, novel antioxidant agents for the treatment of many diseases.

**Keywords:** Gas chromatography and mass spectroscopy, methanolic extract, pharmaceutical importance, phytochemicals, *Terminalia coriacea*.
Lost wax-bolus technique to process closed hollow obturator with uniform wall thickness using single flasking procedure

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Abstract
Introduction: Maxillary obturator prosthesis is more frequent treatment modality than surgical reconstruction for maxillectomy in patients suffering from oral cancer. The obturators often become heavy and hence are hollowed out in the defect portion to reduce its weight as a standard practice.

Materials and Methods: The processing technique described the incorporation of the preshaped “waxbolus” during packing procedure of the Obturator prosthesis and eliminated later by melting it once the curing procedure is completed.

Results: This article is a single step procedure resulting into the closed-hollow obturator as single unit with uniform wall thickness around the hollow space ensuring the least possible weight of the hollow obturator.

Conclusion: This processing technique achieves predictable internal dimension of the hollow space providing uniform wall thickness of the obturator.

Keywords: Hollow obturator, maxillectomy, obturator processing technique, oral cancer, retention of prosthesis.
Two colored dental surveying tool as an alternative for carbon marker

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Abstract
Various tools are used with a dental surveyor, including analyzing rods, carbon markers, undercut gauges, and protective sheaths for a specific function. A carbon marker is a parallel-sided carbon rod used to mark the survey line on a cast or a crown on a cast. The carbon marker (with or without protective sheath) cannot differentiate more than one survey line on the cast if needed. The wear of the carbon marker along the parallel walls after repeated use may give an incorrect survey line. We suggest a simple modification in the analyzing rod to prepare a two-colored surveying tool. An analyzing rod is a parallel-sided rod used to analyze the relative parallelism of two or more surfaces of a cast and to mark survey lines on wax patterns. With the modified analyzing rod, the survey lines can be marked with two colors, and the problem of breaking of the carbon marker also can be eliminated.

Keywords: Dental surveyor, dental surveying and designing, removable partial denture.
Abstract
Background: To quantify participation in dental research activities in Malaysia, and investigate its association with socio-demographic and professional characteristics, and perceptions of research and development (R&D) culture.

Materials and Methods: Dental academics in Malaysian dental schools were invited to complete a questionnaire by email and post. The survey comprised questions on research activities in the past 12 months, socio-demographic and professional characteristics, and the R&D Culture Index. Principal components factor analysis was carried out to confirm the factor structure of the R&D Culture Index. Chi-square test was used to identify association of research activities with R&D culture, and socio-demographic and professional characteristics. Binary logistic regression was carried to identify predictors of research activities.

Results: Of 256 potential participants contacted, 128 (50%) useable responses were returned. Three R&D Culture factors accounting for 57.4% of variance were extracted. More positive perception of R&D Support was associated with Malaysians (0.025) and those employed in Government schools (0.017). R&D Skills and Aptitude were associated with older respondents (0.050), PhD qualification (0.014) and more years in academia (0.014). R&D Intention was associated with any of the socio-demographic characteristics. Thirty (23.4%) respondents reported a peer-review research publication in the past 12 months, which was associated with having a PhD (OR 12.79, CI 1.28-127.96), after adjustment in regression analyses.

Discussion: Postgraduate research training should be encouraged to promote participation in research activities. R&D culture did not appear to impact on research productivity. Other factors such as individual attitudinal interests should be studied.

Keywords: Faculty development, Research and development, Research productivity.

Transcriptome sequencing of an Antarctic microalga, Chlorella sp. (Trebouxiophyceae, Chlorophyta) subjected to short-term ultraviolet radiation stress

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Abstract
Stratospheric ozone depletion has led to increasing levels of ultraviolet radiation (UVR) reaching the Earth’s surface. Elevated UVR, particularly in the high latitudes, potentially causes shifts in species composition and diversity in various ecosystems, consequently altering the biogeochemical cycles. Microalgae are not only ecologically important as primary producers, generating atmospheric oxygen and sequestering carbon dioxide; they are also economically important as sources of health supplement, pigments, biofuel and others. Changes to the size and composition of algal communities can lead to profound impacts to the fisheries productivity. There have been studies on the effects of UVR on the growth, photosynthesis and biochemical composition of microalgae, but limited information on the underlying molecular mechanisms involved in the response and adaptation of microalgae to UVR is available. We employed RNA-seq to quantitatively evaluate and compare the transcriptomes of an Antarctic freshwater Chlorella sp. grown at ambient versus elevated UVR conditions. Differentially expressed genes, relating to the fatty acid degradation, amino acid metabolism, starch and sucrose metabolism and peroxisome pathways, suggest conservation and remobilisation of energy resources, maintenance of newly synthesised protein and inhibition of protein degradation, ensuring membrane lipid homeostasis and regulating antioxidative mechanisms, as the acclimation strategies in response to UVR. These findings expand current knowledge of gene expression in polar Chlorella sp. in response to short-term UVR. Studies on stress tolerance mechanisms are important to understand and predict future impacts of climate change. Genes, proteins and pathways identified from these adaptable polar algae have potentially far-reaching biotechnological applications.

Keywords: Fatty acid degradation, Peroxisome, RNA-seq, Starch and sucrose metabolism.

**Effect of non-surgical periodontal therapy on the leukocyte cell count and protein levels in peripheral blood of periodontitis patients**

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**Abstract**

**Background:** The aim of this study was to evaluate the effect of scaling and root planing (SRP) on the level of systemic inflammatory markers in the peripheral blood comprising total and differential leukocyte count, serum albumin, globulin and albumin/ globulin (A/G) ratio.

**Materials and Methods:** 30 subjects with periodontitis were selected for this study. Clinical parameters such as plaque index (PI), gingival index (GI) and pocket depth (PD) were examined. Blood cell variables, including hemoglobin, total leukocyte count, neutrophil and lymphocyte count, including total protein; albumin, globulin and A/G ratio were analyzed. All the subjects received non surgical periodontal therapy. The patients were recalled at three and six weeks for reassessment of clinical parameters and blood cell variables.

**Results:** Periodontal inflammation may be associated with increased lymphocyte, total protein and serum globulin while decrease in serum albumin and A/G ratio and this finding corresponded with GI and PI. SRP resulted in statistically significant reduction in PI (p<0.001), GI (p<0.001), PD (p<0.001), serum globulin (p<0.007), total protein (p<0.001) and lymphocyte (p=0.015) and increase in hemoglobin (p=0.01), serum albumin (p<0.001) and A/G ratio (< 0.001) at 3 and 6 weeks from baseline.

**Conclusion:** Periodontitis patient may have elevated levels of peripheral lymphocyte number, serum globulin and total protein as well as decreased serum albumin and A/G ratio. These changes might be associated with severity of disease and SRP lowered the level of peripheral lymphocyte number and globulin level and improved the serum albumin and A/G ratio.

**Keywords:** Hemoglobin, Leukocyte, Periodontitis, Serum protein, White blood cell.
Differential regulation of cell death pathways by the microenvironment correlates with chemoresistance and survival in leukaemia

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Abstract

Glucocorticoids (GCs) and topoisomerase II inhibitors are used to treat acute lymphoblastic leukaemia (ALL) as they induce death in lymphoid cells through the glucocorticoid receptor (GR) and p53 respectively. Mechanisms underlying ALL cell death and the contribution of the bone marrow microenvironment to drug response/resistance remain unclear. The role of the microenvironment and the identification of chemoresistance determinants were studied by transcriptomic analysis in ALL cells treated with Dexamethasone (Dex), and Etoposide (Etop) grown in the presence or absence of bone marrow conditioned media (CM). The necroptotic (RIPK1) and the apoptotic (caspase-8/3) markers were downregulated by CM, whereas the inhibitory effects of chemotherapy on the autophagy marker Beclin-1 (BECN1) were reduced suggesting CM exerts cytoprotective effects. GCs upregulated the RIPK1 ubiquitinating factor BIRC3 (cIAP2), in GC-sensitive (CEM-C7-14) but not in resistant (CEM-C15) cells. In addition, CM selectively affected GR phosphorylation in a site and cell-specific manner. GR is recruited to RIPK1, BECN1 and BIRC3 promoters in the sensitive but not in the resistant cells with phosphorylated GR forms being generally less recruited in the presence of hormone. FACS analysis and caspase-8 assays demonstrated that CM promoted a pro-survival trend. High molecular weight proteins reacting with the RIPK1 antibody were modified upon incubation with the BIRC3 inhibitor AT406 in CEM-C7-14 cells suggesting that they represent ubiquitinated forms of RIPK1. Our data suggest that there is a correlation between microenvironment-induced ALL proliferation and altered response to chemotherapy.
Chemical composition and wound healing activity of methanolic leaf extract of *Hydrolea zeylanica* Vahl. by in vivo excision and incision models

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**Abstract**

**Background:** *Hydrolea zeylanica* L. leaves are used traditionally for burns, wounds, antiseptic, and callus ulcers.

**Objective:** The objective of the study was to discuss chemical composition and to evaluate the wound healing property of *H. zeylanica* L. methanol extract (HZLME) on rats using excision and incision wound models.

**Materials and Methods:** Wistar albino rats (150-200 g) were divided into four groups (*n* = 6). Group I negative control (Water-soluble ointment base), Group II standard (povidone iodine [5% w/w] ointment), Group III Test I - HZLME ointment (5% w/w), and Groups IV Test II - *H. zeylanica* leaf aqueous extract ointment (5% w/w) were applied topically. In incision wound models, the treatment was given for 10 days from the day of wound; skin breaking strength was estimated in incision wound model. In excision wound model, treatment continued until wound is completely healed. Rate of wound contraction and period of epithelization was evaluated thereafter. The data were analyzed by one-way ANOVA, followed by Dunnett’s test.

**Results:** Gas chromatography-mass spectrometry chromatogram analysis of the HZLME showed several peaks indicating the presence of various phytochemical constituents. HZLME increased the rate of wound contraction, decreased the period of epithelization and increased skin breaking strength.

**Conclusion:** The use of *H. zeylanica* in various skin diseases has been proved by this work, as it showed a wound healing potential.

**Keywords:** Epithelization, gas chromatography-mass spectroscopy analysis, *Hydrolea zeylanica*, skin breaking strength, wound healing.

Transdermal delivery of tolterodine tartrate for overactive bladder treatment: In vitro and in vivo evaluation

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Abstract
The purpose of the study was to develop a transdermal tolterodine tartrate (TT) patch and to analyse its efficacy for overactive bladder (OAB) treatment. Patches were prepared using various polymers and plasticizers via the solvent casting method. The patches were characterized for tensile strength, thickness, moisture content, modulus of elasticity and water absorption capacity. Differential scanning calorimetry and Fourier transform infrared analyses were also performed. To determine patch effectiveness, in vitro release, permeation and animal studies were performed. The patches showed satisfactory percentage of release, up to 89.9%, and their mechanical properties included thickness (0.10–0.15 mm), tensile strength (4.62–9.98 MPa) and modulus of elasticity (20–29 MPa). There were no significant interactions between TT and other excipients. Animal studies indicated that the TT patch reduced the incidence of side effects; however, studies of longer duration are required to determine the effectiveness in treating OAB.

Keywords: tolterodine tartrate, transdermal, overactive bladder, matrix patches, permeation.
A quantitative insight on preclinical and clinical year medical students towards adverse drug reporting and pharmacovigilance in Malaysia

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Abstract
Objective: To investigate the knowledge of medical students and their perception on adverse drug reaction (ADR) reporting and pharmacovigilance.

Methods: Cross-sectional study was carried out on clinical or preclinical year medical students using paper-based questionnaires during their coursework.

Key findings: There were differences between the two groups in responses relating to ADR reporting (preclinical 3.3 versus clinical 3.7; P < 0.01) and reasons for not reporting a suspected ADR (preclinical 3.4 versus clinical 3.8; P = 0.001).

Conclusions: Medical students from clinical years had higher knowledge of ADR reporting. The perception on ADR reporting by clinical year students was significantly higher.

Keywords: adverse drug reactions, Malaysia, medical students, pharmacovigilance.

**Knowledge about human papillomavirus and cervical cancer: Predictors of HPV vaccination among dental students**

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**Abstract**

**Background:** The objective of this study is to determine the influence of dental students’ knowledge and attitude regarding human papillomavirus infection of cervical cancer on willingness to pay for vaccination.

**Basic research design:** A convenience sampling method was used. The minimal sample size of 136 was calculated using the Raosoft calculator with a 5 % margin of error and 95% confidence level.

**Participants:** The study population were all final year dental students from the School of Dentistry.

**Methods:** A self-administered questionnaire was used to measure knowledge levels and attitudes regarding human papillomavirus vaccination. Contingent valuation was conducted for willingness to pay for vaccination.

**Main outcome measures:** The Center for Disease Control and Prevention has stated that human papillomavirus are associated with oropharynx cancer and the American Dental Association insist on expanding public awareness of the oncogenic potential of some HPV infections. Thus, as future dental practitioners, dental students should be aware of human papillomavirus and their links with cancer and the benefits of vaccination. Results: Knowledge on HPV and cervical cancer did not impact on attitudes towards vaccines. However, significant correlation existed between knowledge and willingness to pay for vaccination.

**Conclusions:** Dental students’ knowledge on HPV and cervical cancer has no influence on their attitude towards HPV vaccines. However, their willingness to pay for HPV vaccination is influenced by their knowledge of cervical cancer and HPV vaccination.

**Keywords:** Dental students, Malaysia, Willingness to pay, HPV vaccine, cervical cancer.

**Quality of life and caregivers' burden of Parkinson’s disease**

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**Abstract**

**Aim:** This study focused on the impact of the clinical features on the quality of life (QoL) of Parkinson's disease (PD) patients and of their caregivers.

**Methods:** This study included PD patients along with their caregivers and was undertaken at the Malaysian Parkinson's Disease Association from June 2016 to November 2016. Clinical features of PD patients were assessed using the Movement Disorder Society revised Unified Parkinson Disease Rating Scale; the Hoehn and Yahr stage and the Schwab and England Activities of Daily Living Scale were used to assess the severity and the ability of PD patients respectively. QoL of PD patients was measured using the Parkinson's Disease Questionnaire-39 (PDQ-39). The revised version of the Zarit Burden Interview assessed caregiver burden.

**Results:** At least one of the clinical features affected PD patients' QoL, and at least one of the QoL domains affected the caregivers' burden. Clinical features "saliva and drooling" and "dyskinesia" explained 29% of variance in QoL of PD patients. The QoL domains "stigma," along with "emotional well-being" explained 48.6% of variance in caregivers' burden.

**Conclusions:** The clinical features "saliva and drooling" and "dyskinesia" impacted the QoL of PD patients, and the QoL domains "stigma" and "emotional well-being" of PD patients impacted their caregivers' burden.

**Keywords:** Carers, Malaysia, Quality of life, Clinical features, Correlations.
Neglected intestinal parasites, malnutrition and associated key factors: A population based cross-sectional study among indigenous communities in Sarawak, Malaysia

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Abstract

Intestinal parasitic infections (IPIs) have been recognized as one of the most significant causes of illness among disadvantaged communities. Many studies have been conducted on the prevalence of IPIs in Malaysia. However, these studies mostly focused on the indigenous groups in Peninsular Malaysia. The present study was conducted to provide the current baseline data on prevalence of IPIs, anaemia, malnutrition and associated risk factors among the indigenous communities in Sarawak, situation at northwest Borneo island of Malaysia. A cross sectional study was conducted among the longhouses communities. Stool samples were obtained and examined for the presence of IPIs using microscopy technique. Haemoglobin measurement was done using a portable haemoglobin analyzer. Malnutrition (i.e., stunting, underweight and wasting) was assessed using the WHO Anthro software. Statistical analysis was carried out using SPSS software. A total of 341 participants took part in this study. The overall prevalence of IPIs was 57.5%. Multivariate analysis indicated that the absence of toilets (OR = 1.6; 95% CI = 1.1±2.7; p = 0.002) and close contact with animals (OR = 1.8; 95% CI = 1.3±2.9; p = 0.027) as significant predictors for IPIs. The incidence of anaemia was 36.4%. The incidence of underweight, wasting and stunting were 22.2%, 5.6% and 35.4%, respectively. Multivariate analysis demonstrated that low level of parental education attainment (OR = 1.9; 95% CI = 1.2±3.0; p = 0.006) was identified as significant predictor for anaemia. The incidence of wasting was significantly associated with mild anaemia (OR = 1.2; 95% CI = 0.9±1.7; p = 0.024). Low household income was identified as significant predictor for stunting (OR = 2.1; 95% CI = 9.8±22.2; p = 0.001) and underweight (OR = 1.9; 95% CI = 5.6±18.7; p = 0.037), respectively. Essentially, the present study highlighted that intestinal parasitic infections, anaemia and malnutrition are still prevalent among rural indigenous community in Sarawak. Improvement of socioeconomic status, periodic mass deworming, iron supplementation and health education program should be included in the control and prevention of public health strategies.
Estimation of oxygen diffusing conductance in different dissection portion of the placental cotyledon of passive smoking mothers

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Abstract
A study was undertaken to estimate the amount oxygen that can diffuse across the placenta of the passive smoking mothers in an Indo-Asian population. A total of 24 human term placentas, 11 from mothers exposed to tobacco smoke and 13 from those not exposed to tobacco smoke were collected for estimating weight, surface area and volume term placentas. Five placentas from each of the groups were used for estimating the various parameters for calculating the oxygen-diffusing conductance. A random sampling technique at 7 levels of tissue preparation was adopted. Cotyledons were cut into blocks and each block was further cut into upper (maternal), middle (foeto-maternal) and lower (foetal) components. Semithin sections, 1 μm thick, stained using a modified toluidine was viewed and the images were analysed. A Merz grid was used to estimate the vascular volumes, exchange surface areas and tissue diffusion distances for calculation the oxygen-diffusing conductance of the placenta. These were combined with physicochemical quantities (oxygen-haemoglobin reaction rates and tissues oxygen diffusion coefficients) obtained from literature in order to estimate the partial conductance of the six tissue compartments of the oxygen pathway. The present study demonstrates that there is no significant difference in the total oxygen-diffusing conductance in the placenta of passive smokers and those not exposed to tobacco smoke. However, the significant increase in the foetal capillaries and foetal erythrocytes conductance suggests that an adaptive mechanism in the foetal part of the placenta may be occurring to ensure adequate oxygen to the foetus.
Acinetobacter spp. infections in Malaysia: A review of antimicrobial resistance trends, mechanisms and epidemiology

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Abstract

Acinetobacter spp. are important nosocomial pathogens, in particular the Acinetobacter baumannii-calcoaceticus complex, which have become a global public health threat due to increasing resistance to carbapenems and almost all other antimicrobial compounds. High rates of resistance have been reported among countries in Southeast Asia, including Malaysia. In this review, we examine the antimicrobial resistance profiles of Acinetobacter spp. hospital isolates from Malaysia over a period of nearly three decades (1987–2016) with data obtained from various peer-reviewed publications as well as the Malaysian National Surveillance on Antibiotic Resistance (NSAR). NSAR data indicated that for most antimicrobial compounds, including carbapenems, the peak resistance rates were reached around 2008–2009 and thereafter, rates have remained fairly constant (e.g., 50–60% for carbapenems). Individual reports from various hospitals in Peninsular Malaysia do not always reflect the nationwide resistance rates and often showed higher rates of resistance. We also reviewed the epidemiology and mechanisms of resistance that have been investigated in Malaysian Acinetobacter spp. isolates, particularly carbapenem resistance and found that blaoxa-23 is the most prevalent acquired carbapenemase-encoding gene. From the very few published reports and whole genome sequences that are available, most of the Acinetobacter spp. isolates from Malaysia belonged to the Global Clone 2 (GC2) CC92 group with ST195 being the predominant sequence type. The quality of data and analysis in the national surveillance reports could be improved and more molecular epidemiology and genomics studies need to be carried out for further in-depth understanding of Malaysian Acinetobacter spp. isolates.
Antibacterial effects of natural herbal extracts on *Streptococcus mutans*: Can they be potential additives in dentifrices?

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Abstract

**Background:** Many plants or herbs exhibit potent antimicrobial activity against various microorganisms. They have no side effects and presumably act against and modulate the factors that are crucial for microbial survival or their activity. *Streptococcus mutans* is a pioneer bacteria implicated in dental caries. This study aims to evaluate the antimicrobial activity of garlic bulbs, pudina leaves, and mango and eucalyptus twig extracts on *Streptococcus mutans* by evaluating their zone of inhibition and determining their minimum inhibitory concentration (MIC).

**Method:** Microbiological assay (well diffusion method) to determine zone of inhibition against pure forms of *Streptococcus mutans* was performed. The antibacterial effects of methanolic extracts of mango twigs, eucalyptus twigs, pudina leaves, and garlic bulbs were studied. Test compounds were further evaluated for their MIC.

**Results:** Extracts derived from mango and eucalyptus twigs showed significant antibacterial effects at test concentrations. Pudina and garlic extracts did not show any significant antibacterial effects at similar concentrations. Upon further evaluation of the 2 positive compounds for their MIC, mango twigs demonstrated more antimicrobial potential than eucalyptus twigs at a lower concentration.

**Conclusion:** Our observations indicated that the mango twig extracts possess higher antibacterial effects against *Streptococcus mutans* than other compounds at specific test concentration.
Rawal SY and Rawal YB. Angioleiomyoma (vascular leiomyoma) of the oral cavity. *Head and Neck Pathology*, 2017; Doi: 10.1007/s12105-017-0827-9. [Epub ahead of print]. (CiteScore: 2.16; Tier: Q1).

**Angioleiomyoma (vascular leiomyoma) of the oral cavity**

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**Abstract**

A 70-year-old male presented with a slow growing, dome shaped and painless mass of the hard palate. The mass was excised. Histopathological examination confirmed the diagnosis of a angioleiomyoma (vascular leiomyoma). A leiomyoma is an uncommon benign tumor of smooth muscle differentiation. True leiomyomas of the oral cavity are rare and most oral tumors are derived from the smooth muscle of walls of blood vessels. Therefore, they are called vascular leiomyomas or angioleiomyomas. Clinically, they may resemble a myriad other conditions both benign and malignant. A definitive diagnosis depends upon histopathological examination of the biopsied tissue in correlation with the tumor cell immunohistochemistry. Tumors are excised and recurrence is rare. The histopathological findings and differential diagnosis of a case of a palatal angioleiomyoma are discussed.

**Keywords:** Oral, Vascular, Leiomyoma, Angioleiomyoma, Tumor, SMA.
Transplantation of human bone marrow mesenchymal stromal cells reduces liver fibrosis more effectively than Wharton’s jelly mesenchymal stromal cells

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Abstract

Background: Mesenchymal stromal cells (MSCs) from various tissues have shown moderate therapeutic efficacy in reversing liver fibrosis in preclinical models. Here, we compared the relative therapeutic potential of pooled, adult human bone marrow (BM) and neonatal Wharton’s jelly (WJ)-derived MSCs to treat CCl4-induced liver fibrosis in rats.

Methods: Sprague-Dawley rats were injected with CCl4 for 8 weeks to induce irreversible liver fibrosis. Ex-vivo expanded, pooled human MSCs obtained from BM and WJ were intravenously administered into rats with liver fibrosis at a dose of 10 x 106 cells/animal. Sham control and vehicle-treated animals served as negative and disease controls, respectively. The animals were sacrificed at 30 and 70 days after cell transplantation and hepatic-hydroxyproline content, histopathological, and immunohistochemical analyses were performed.

Results: BM-MSCs treatment showed a marked reduction in liver fibrosis as determined by Masson’s trichrome and Sirius red staining as compared to those treated with the vehicle. Furthermore, hepatic-hydroxyproline content and percentage collagen proportionate area were found to be significantly lower in the BM-MSCs-treated group. In contrast, WJ-MSCs treatment showed less reduction of fibrosis at both time points. Immunohistochemical analysis of BM-MSCs-treated liver samples showed a reduction in α-SMA+ myofibroblasts and increased number of EpCAM+ hepatic progenitor cells, along with Ki-67+ and human matrix metalloprotease-1+ (MMP-1+) cells as compared to WJ-MSCs-treated rat livers.

Conclusions: Our findings suggest that BM-MSCs are more effective than WJ-MSCs in treating liver fibrosis in a CCl4-induced model in rats. The superior therapeutic activity of BM-MSCs may be attributed to their expression of certain MMPs and angiogenic factors.

Keywords: Human BM- and WJ-MSCs, Liver fibrosis, MMPs, Angiogenesis.
NMDA receptor antagonism with novel indolyl, 2-(1,1-Dimethyl-1,3-dihydro-benzo[e]indol-2-ylidene)-malonaldehyde, reduces seizures duration in a rat model of epilepsy

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Abstract

N-methyl-D-aspartate receptors (NMDAR) play a central role in epileptogenesis and NMDAR antagonists have been shown to have antiepileptic effects in animals and humans. Despite significant progress in the development of antiepileptic therapies over the previous 3 decades, a need still exists for novel therapies. We screened an in-house library of small molecules targeting the NMDA receptor. A novel indolyl compound, 2-(1,1-Dimethyl-1,3-dihydro-benzo[e]indol-2-ylidene)-malonaldehyde, (DDBM) showed the best binding with the NMDA receptor and computational docking data showed that DDBM antagonised the binding sites of the NMDA receptor at lower docking energies compared to other molecules. Using a rat electroconvulsive shock (ECS) model of epilepsy we showed that DDBM decreased seizure duration and improved the histological outcomes. Our data show for the first time that indolyls like DDBM have robust anticonvulsive activity and have the potential to be developed as novel anticonvulsants.

Emerging potential of stimulus-responsive nanosized anticancer drug delivery systems for systemic applications

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Abstract
The development of novel drug delivery systems based on well-defined polymer therapeutics has led to significant improvements in the treatment of multiple disorders. Advances in material chemistry, nanotechnology, and nanomedicine have revolutionized the practices of drug delivery. Stimulus-responsive material-based nanosized drug delivery systems have remarkable properties that allow them to circumvent biological barriers and achieve targeted intracellular drug delivery. Specifically, the development of novel nanocarrier-based therapeutics is the need of the hour in managing complex diseases. In this review, we have briefly described the fundamentals of drug targeting to diseased tissues, physiological barriers in the human body, and the mechanisms/modes of drug-loaded carrier systems. To that end, this review serves as a comprehensive overview of the recent developments in stimulus-responsive drug delivery systems, with focus on their potential applications and impact on the future of drug delivery.

Keywords: Drug delivery systems, Nanomedicine, Polymer therapeutics, Stimulus-responsive.
Sahu PS, Lim YAL, Mahmud R, Somanath SD, Tan CT, Ramachandran CP. Needs of exploring the burden of recent onset seizures due to neurocysticercosis and challenges in southeast Asia focusing on scenario in Malaysia. *Asian Pacific Journal of Tropical Medicine*, 2017; 10(4): 332–340. (ISI IF: 0.925; CiteScore: 2.16; Tier: Q1).

**Needs of exploring the burden of recent onset seizures due to neurocysticercosis and challenges in southeast Asia focusing on scenario in Malaysia**

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**Abstract**

Seizures due to neurocysticercosis (NCC) is a neglected human-to-human transmitted disorder and an emerging problem worldwide. A substantial portion of recent onset seizures is known to be attributed to NCC in *Taenia solium* (*T. solium*) endemic areas where populations which neither raise pigs nor eat pig meat are also at risk. High prevalence of NCC causing epilepsy has been reported in the underdeveloped areas of Southeast Asia (SEA) however, only fragmentary information on its incidence is available in countries like Malaysia. In Malaysia *T. solium* infection was previously thought to be infrequent due to Muslim population majority and the religious prohibition of consuming pork, but it is not totally absent. There is an evident lack of knowledge and awareness of the actual burden, routes of transmission, and the impact of NCC in this region. The problem is assumed to be more prevalent particularly in cities because of the frequent inflow of possibly *T. solium* infected individuals or carriers among those who migrate from neighboring endemic countries to Malaysia. The issue of imported cases that are likely to be emerging in Malaysia is highlighted here. An accurate quantification of regional burdens of epilepsy due to NCC in Malaysia is warranted considering the disease emergence in its neighboring countries. It is suggested that the importance of NCC be recognized through quantification of its burden, and also to collect epidemiological data for its subsequent elimination in line of World Health Organization’s mission for control of cysticercosis as a neglected tropical disease. In this review the need as well as a strategy for neuro-care center screening of epilepsy cases, and various issues with possible explanations are discussed. It is also proposed that NCC be declared as a reportable disease which is one of the eradicable public health problems in SEA.

**Keywords:** Seizure, Recent onset seizure, NTD, Cysticercosis, Neurocysticercosis, Southeast Asia.
Bilateral fracture of prostheses post-hip replacement. Case Report

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Abstract
Fracture of hip prostheses is a rare occurrence. A case of bilateral hip prostheses fracture is described here. The need to follow-up and remain vigilant post hip replacement is highlighted.

Keywords: Bilateral hip replacement, prostheses fracture.
Bioactivity of *Mesona palustris* (Black Cincau) as a nutraceutical agent

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**Abstract**

*Mesona palustris*, colloquially known as ‘Black Cincau’, can commonly be found in East and South East Asian regions. Traditionally, *M. palustris* extracts have been used as herbal drinks to promote vitality and health. With advancements in technology, *M. palustris* may now be processed into more nutraceutical options, including edible jellies. Studies have also come up with efficient extraction processes to better characterize its chemical constituents. Containing phenolic compounds like flavonoid and tannins, *M. palustris* has recently been reported to yield many exciting pre-clinical observations that are comparable to bioactive metabolites found in plants from the same genus, including *Mesona procumbens* and *Mesona chinensis*, alongside unrelated herbaceous plant species which have been utilized as natural remedy options. Thus, this review discusses the recently observed pre-clinical applications of *M. palustris* by highlighting its ability in promoting antidiabetic, anticancer, and antihypertensive properties, which are closely tied to its antioxidative nature. Given the developing nature of *M. palustris* utilization in pre-clinical and possibly clinical research, more thorough characterization, pharmacological, and molecular studies should be conducted not only to avoid adverse risks or derogatory interactions with existing drugs, but also to properly direct its use as a nutraceutical agent for specific indications.

**Keywords:** antioxidative, black cincau, flavonoids, natural product, nutraceuticals, phenolic compounds.
Biomarkers and therapeutic advances in glioblastoma multiforme

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Abstract
Glioblastoma multiforme (GBM) is a malignant tumor within the brain. Generally classified as primary and secondary with several different subtypes, ample molecular biomarkers have risen throughout the years which have garnered the attention of researchers. The advancements in genomics and proteomics have allowed researchers to gather prominent molecular biomarkers. All these biomarkers are gathered by means of biopsy or bodily fluid sample collection and are quantitatively analyzed by polymerase chain reaction coupled with other computational technologies. This review highlights the significance, regulation and prevalence of molecular biomarkers such as O⁶-methylguanine-DNA methyltransferase, epidermal growth factor receptor vIII, isocitrate dehydrogenase mutation and several others which expressed differently in different types and molecular subtypes of GBM. The discoveries and roles of GBM-specific microRNAs including miR-21 and miR-10b as biomarkers with promising prognostic values were also delineated. The role and mechanism of biomarkers in GBM tumorigenesis are essential in the development of therapy for patients suffering from the disease itself. Thus, this review also discusses the mechanisms, effects and limitations of therapy such as temozolomide, viral gene transfer, biomarker-based vaccines or even engineered T cells for more specific responses. Biomarkers have displayed a high value and could eventually be utilized as drug targets. It is hoped that by combining different aspects of the disease which present with different biomarkers could lead to the development of a robust, effective and innovative take on GBM therapy.

Keywords: biomarkers, cancer therapy, glioblastoma, microRNA, temozolomide.

**Placebo controlled trials: Interests of subjects versus interests of drug regulators**

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**Abstract**

The use of placebo-controlled trials in situations where established therapies are available is considered ethically problematic since the patients randomised to the placebo group are deprived of the beneficial treatment. The pharmaceutical industry and drug regulators seem to argue that placebo-controlled trials with extensive precautions and control measures in place should still be allowed since they provide necessary scientific evidence for the efficacy and safety of new drugs. On the other hand, the scientific value and usefulness for clinical decision-making may be much higher if the new drug is compared directly to existing therapies. As such, it may still be unethical to impose the burden and risk of placebo-controlled trials on patients even if extensive precautions are taken. A few exceptions do exist. The use of placebo-controlled trials in situations where an established, effective and safe therapy exists remains largely controversial.

**Keywords:** randomised controlled trial, placebo, research ethics, ethics, institutional review board, ethics committee.
A qualitative study on pharmacists’ perception on integrating pharmacists into private general practitioner’s clinics in Malaysia

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Abstract

Background: Private general practitioners in Malaysia largely operates as solo practices – prescribing and supplying medications to patients directly from their clinics, thus posing risk of medication-related problems to consumers. A pharmacy practice reform that integrates pharmacists into primary healthcare clinics can be a potential initiative to promote quality use of medication. This model of care is a novel approach in Malaysia and research in the local context is required, especially from the perspectives of pharmacists.

Objective: To explore pharmacists' views in integrating pharmacists into private GP clinics in Malaysia.

Methods: A combination of purposive and snowballing sampling was used to recruit community and hospital pharmacists from urban areas in Malaysia to participate either in focus groups or semi-structured interviews. A total of 2 focus groups and 4 semi-structured interviews were conducted. Sessions were audio recorded, transcribed verbatim and thematically analysed using NVivo 10.

Results: Four major themes were identified: (1) Limited potential to expand pharmacists’ roles, (2) Concerns about non-pharmacists dispensing medicines in private GP clinics, (3) Lack of trust from consumers and private GPs, (4) Cost implications. Participants felt that there was a limited role for pharmacists in private GP clinics. This was because the medication supply role is currently undertaken in private GP clinics without the need of pharmacists. The perceived lack of trust from consumers and private GPs towards pharmacists arises from the belief that healthcare is the GPs’ responsibility. This suggests that there is a need for increased public and GP awareness towards the capabilities of pharmacists’ in medication management. Participants were concerned about an increase in cost to private GP visits if pharmacists were to be integrated. Nevertheless, some participants perceived the integration as a means to reduce medical costs through improved quality use of medicines.

Conclusion: Findings from the study provided a better understanding to help ascertain pharmacists’ views on their readiness and acceptance in a potential new model of practice.

Keywords: Pharmacists, Physicians, Primary Health Care, Delivery of Health Care, Integrated, Interprofessional Relations, Qualitative Research, Malaysia.
Exploring the role of pharmacists in private primary healthcare clinics in Malaysia: The views of general practitioners

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Abstract

Background: Private general practitioners (GPs) in Malaysia mainly operate solo practices with little interdisciplinary collaboration or co-ordination with other healthcare providers which potentially fragments and limits patient care. Pharmacists as medication experts can contribute to the private primary care sector using their influence to ensure quality use of medicines.

Aim: To explore the views of private GPs in Malaysia on integration of pharmacists into private primary healthcare clinics.

Method: A combination of purposive and snowballing sampling was used to recruit private sector GPs to participate in focus groups and semi-structured interviews in Malaysia. Sessions were audio recorded, transcribed verbatim and thematically analysed using NVivo 10.

Results: Thirteen private GPs participated in one focus group and ten semi-structured interviews. Four major themes were identified: (i) poor understanding of pharmacists' roles; (ii) readiness to accept pharmacists in private primary healthcare clinics; (iii) lack of confidence and trust in pharmacists; and (iv) perceived increased costs with pharmacist integration. Results indicated participants' views and acceptance were largely influenced by the amount of exposure and experience they had working alongside pharmacists. Participants viewed a lack of confidence in pharmacists and increase in costs associated with an employed pharmacist within private primary healthcare clinics as barriers to integration.

Conclusion: Private GPs expressed reservations toward this new model due to the lack of understanding of pharmacists' roles and responsibilities. There is a need for awareness among private GPs on pharmacists' roles to improve their acceptance of the integration of pharmacists into private primary healthcare clinics in Malaysia.

Keywords: integration, pharmacist, general practitioners, primary healthcare clinics, private, Malaysia.
Anemia and iron deficiency in pregnant women attending an antenatal clinic in a Teaching Hospital in Southern Sri Lanka

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Abstract

Introduction: In Sri Lanka the current prevalence of anaemia during pregnancy is estimated to be less than 20%.

Objectives: To determine the rate of anaemia defined as hemoglobin concentration < 11 g/dl, and the rate of iron deficiency using the best cut off level of serum ferritin, in women presenting for antenatal care.

Methods: Three hundred and fifty consecutive pregnant women with gestations between 12 to 20 weeks, presenting to the Academic Obstetric Unit at the Teaching Hospital Mahamodera, Galle, Sri Lanka from 10.11.2014 to 13.01.2015 had their haemoglobin and hematocrit measured by flowcytometry and hydro-dynamic focusing methods using a Sysmex- XS-500i System and serum ferritin measured by electro-chemiluminescence method using a Cobas-e411 Analyzer. The rate of anaemia was calculated. The best cut off level of serum ferritin for the detection of anaemia was obtained using a Receiver Operator Characteristics (ROC) curve, and using this cut off, the rate of iron deficiency was calculated.

Results: The rate of anaemia was 16.6%. The best cut off level of serum ferritin for the detection of anaemia was < 30 μg/L (the area under the ROC curve was 0.77; 95% CI -0.72 to0.81), with a sensitivity of 78.3% (95% CI 65.8 - 87.9) and a specificity of 74% (95% CI 68.6 -79.0) in detecting anaemia. Using this cut off, 36.9% of the pregnant women had iron deficiency.

Conclusion: Rates of anaemia (16.6%) and iron deficiency (36.9%) in pregnancy are at levels of mild to moderate public health significance respectively.
Identification of the antagonistic effect of (-) carvone on Ca2+ channel, histamine and acetylcholine-muscarinic receptors in isolated smooth muscle preparation: An in vitro and in silico correlation study

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Abstract
Carvone is a monoterpene found mainly in caraway seeds, dill and fennel fruits. These are used as a folk remedy for diarrhoea, acidity and other gastric disorders. The study was designed to evaluate the pharmacological effect of (-)Carvone mediated through L-Type voltage dependant Calcium [Ca++] channel, Histamine [H1] and Muscarinic [M3] receptor on Isolated smooth muscle preparation by Dale’s apparatus and its in –silico correlation. There are two phases in this study, in phase one, the antagonist effect of (-)Carvone on H1, M3 receptor and L-Type voltage gated Ca++channel on isolated chicken ileum preparation by using Dale’s apparatus. In phase two, to gain better insight for the interactions between the compounds and their respective targets along with (-) Carvone, we docked and validated its results based on scoring function using AUTODOCK 1.5.6. Here (-)Carvone showed the binding energy value of -7.53 Kcal/mol for Ca++ protein, -6.33 Kcal/mol for H1 receptor, -5.82 Kcal/mol for M3 receptor. It involves the active site residues and a crucial H-Bond interaction of key residues of LYS97, TYR431 and SER151 respectively. This results confirms that (-)Carvone docks well when compared to standard Ca++ blockers, anti-Histaminic drugs and anti-muscarinic drugs. The phase one study revealed that, the maximum inhibitory action was produced by (-)Carvone against Calcium ion, followed by acetylcholine and Histamine on isolated smooth muscle. The study shows, (-)Carvone produces antagonist effect by multi receptor mechanism against H1, M3 receptor and Ca++ so it may inhibit eosinophil, chemotaxis, LTB4 release and various effects on many excitable cells of the body such as cardiac muscle, smooth muscles of blood vessels or neurons. The correlation of in –vitro and in-silico results suggested that (-)Carvone is useful for the treatment of various metabolic disorders and GI related disorders.

Keywords: (-)Carvone, Dale’s apparatus, Calcium channel, Histamine, Muscarinic receptor, AUTODOCK 1.5.6.
Lipid based nanocarriers system for topical delivery of photosensitizers

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Abstract

Topical photodynamic therapy (PDT) is a non-invasive technique used in the treatment of malignant and non-malignant skin diseases. It offers great promise because of its simplicity, enhanced patient compliance, localisation of the photosensitizer, as well as the use of light and oxygen to achieve photocytotoxicity. Despite progress in photosensitizer-mediated topical PDT, its clinical application is limited by poor penetration of photosensitizers through the skin. Therefore, much effort has been made to develop nanocarriers that can tackle the challenges of conventional photosensitizer-mediated PDT for topical delivery. This review discusses recent data on the use of different types of lipid-based nanocarriers in delivering photosensitizer for topical PDT.
Recent advances in non-invasive delivery of macromolecules using nanoparticulate carriers system

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Abstract
Background: The drug delivery of macromolecules such as proteins and peptides has become an important area of research and represents the fastest expanding share of the market for human medicines. The most common method for delivering macromolecules is parenterally. However parenteral administration of some therapeutic macromolecules has not been effective because of their rapid clearance from the body. As a result, most macromolecules are only therapeutically useful after multiple injections, which causes poor compliance and systemic side effects.

Method: Therefore, there is a need to improve delivery of therapeutic macromolecules to enable non-invasive delivery routes, less frequent dosing through controlled-release drug delivery, and improved drug targeting to increase efficacy and reduce side effects.

Result: Non-invasive administration routes such as intranasal, pulmonary, transdermal, ocular and oral delivery have been attempted intensively by formulating macromolecules into nanoparticulate carriers system such as polymeric and lipidic nanoparticles.

Conclusion: This review discusses barriers to drug delivery and current formulation technologies to overcome the unfavorable properties of macromolecules via non-invasive delivery (mainly intranasal, pulmonary, transdermal oral and ocular) with a focus on nanoparticulate carrier systems. This review also provided a summary and discussion of recent data on non-invasive delivery of macromolecules using nanoparticulate formulations.
Nano-carrier enabled drug delivery systems for nose to brain targeting in the treatment of neurodegenerative disorder


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Abstract
A major hurdle for the treatment of neurodegenerative disorders is the inability of drug molecules to cross the blood-brain barrier (BBB). Many anti-Parkinson and anti-Alzheimer drugs lack brain targeting; this impedes their ability to reach maximum effective concentrations in the brain. Many of these drugs possess dose-limiting systemic side-effects which, along with difficult dosage regimens, hinder patient compliance and result in discontinuation of treatment. A number of drug delivery and drug targeting systems have been investigated to increase drug bioavailability and the fraction of the drug accumulated in the targeted area, in order to minimize drug degradation and loss, as well as to reduce harmful side effects. Intranasal delivery has come to the forefront as a method that can bypass the BBB and target drugs directly to the brain as an alternative to invasive methods. However, intranasal delivery presents several barriers such as low permeability of the nasal epithelium, as well as physical or chemical removal of the formulation by mucociliary clearance and enzymatic degradation. Recent advances in nanotechnology offer the potential to overcome these problems. This review compiles recent work that uses nanocarriers to improve the treatment outcomes of neurodegenerative disorders such as Parkinson’s (PD) and Alzheimer’s disease (AD) through nose to brain targeting.

Keywords: Alzheimer’s disease, Intranasal delivery, liposome, Nanoparticles, Nanoemulsion, Parkinson's disease.
Phytosterols as a natural anticancer agent: Current status and future perspective

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Abstract
Phytosterols are naturally occurring compounds in plants, structurally similar to cholesterol. The human diet is quite abundant in sitosterol and campesterol. Phytosterols are known to have various bioactive properties including reducing intestinal cholesterol absorption which alleviates blood LDL-cholesterol and cardiovascular problems. It is indicated that phytosterol rich diets may reduce cancer risk by 20%. Phytosterols may also affect host systems, enabling antitumor responses by improving immune response recognition of cancer, affecting the hormone dependent endocrine tumor growth, and by sterol biosynthesis modulation. Moreover, phytosterols have also exhibited properties that directly inhibit tumor growth, including reduced cell cycle progression, apoptosis induction, and tumor metastasis inhibition. The objective of this review is to summarize the current knowledge on occurrences, chemistry, pharmacokinetics and potential anticancer properties of phytosterols in vitro and in vivo. In conclusion, anticancer effects of phytosterols have strongly been suggested and support their dietary inclusion to prevent and treat cancers.

Keywords: Phytosterols, Dietary phytosterols, Phytosterols and cancer, Campesterol, Anticancer effect of sterols, Dietary phytosterols and cancer.

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Abstract
Type 2 diabetes mellitus (T2DM) is one of the most threatening, non-communicable ailments worldwide. The use of nanoparticles as a medicine in the treatment of T2DM is an attractive proposition. In the current study, zinc oxide nanoparticles (ZnO NPs), cerium oxide nanoparticles (CeO₂ NPs), silver nanoparticles (Ag NPs), and Momordica charantia (MC) were evaluated for their in vivo anti-diabetic activity. The resulting ZnO, CeO₂, and Ag NPs were characterized via various techniques such as XRD, FT-IR, PSA, and SEM. The synthesized NPs and MC extract were tested for toxicity using a sub-acute oral toxicity model by following the OECD 425 guidelines. The male Wistar rats with weights in the range of 180–200 g were grouped as follows: normal control: who did not receive any treatment; diabetic control: who received a single intraperitoneal dose of streptozotocin (40 mg kg⁻¹); standard: who received a single daily oral dose of streptozotocin 50 mg per kg body weight; diabetic and ZnO NPs: who received a single daily oral dose of 100 mg kg⁻¹ and 200 mg kg⁻¹ of ZnO NPs; diabetic and CeO₂ NPs: who received a single daily oral dose of 100 mg kg⁻¹ and 200 mg kg⁻¹ of CeO₂ NPs; diabetic and Ag NPs: who received a single daily oral dose of 100 mg kg⁻¹ and 200 mg kg⁻¹ of Ag NPs; and diabetic and MC: who received a single daily oral dose of 100 mg kg⁻¹ and 200 mg kg⁻¹ of MC. In conclusion, the green-synthesized NPs showed no toxic effect and were considered safe. From the experimental results, it may be concluded that due to the extensive biological and pharmacological properties, the ZnO NPs and Ag NPs had more potent anti-hyperglycemic activity than MC and CeO₂ NPs. Further pharmacokinetic studies are required to establish the exact mechanism of action (of NPs).

**Dendrimer nanoarchitectures for cancer diagnosis and anticancer drug delivery**

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**Abstract**

Dendrimers are novel nanoarchitectures with unique properties including a globular 3D shape, a monodispersed unimicellar nature and a nanometric size range. The availability of multiple peripheral functional groups and tunable surface engineering enable the facile modification of the dendrimer surface with different therapeutic drugs, diagnostic agents and targeting ligands. Drug encapsulation, and solubilizing and passive targeting also equally contribute to the therapeutic use of dendrimers. In this review, we highlight recent advances in the delivery of anticancer drugs using dendrimers, as well as other biomedical and diagnostic applications. Taken together, the immense potential and utility of dendrimers are envisaged to have a significant positive impact on the growing arena of drug delivery and targeting.
Fabrication and characterization of nifedipine loaded β-cyclodextrin nanosponges: An in vitro and in vivo evaluation

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Abstract

Cyclodextrin based nanosponges are gaining much consideration due to their aptitude to augment oral solubility of poorly water-soluble medications such as nifedipine. Here in the contemporary research, diphenyl carbonate was employed for crosslinking the cyclodextrin successfully. DLS studies confirmed particle size in the range of 400–500 nm with monodisperse size distribution. TEM measurement established spherical shape and size range of the nanosuspension. SEM photomicrograph confirmed porous structure of placebo nanosponges while drug loaded nanosponge formulation NS3 revealed solid surface. FTIR studies established no drug-polymer interaction. DSC thermograms showed molecular level dispersion of drug in nanosponges. In vitro drug release exhibited a burst release for first four hours and delivered drug in sustained manner for subsequent 24 h. When encapsulated within nanosponges, oral bioavailability of nifedipine was enhanced in comparison to control formulation (C_{max} for test formulation was 0.2; 0.055 for control). The fabricated nanosponges displayed admirable stability under normal and stress conditions. %Drug entrapment encountered a slight decline (77.33 ± 1.62% to 74.13 ± 1.47%) during storage while %drug release from initial batch was almost identical when compared with stored nanosponges.
Multiple etiologies of infectious diarrhea and concurrent infections in a pediatric outpatient-based screening study in Odisha, India

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Abstract

Background: There are multiple etiologies responsible for infectious gastroenteritis causing acute diarrhea which are often under diagnosed. Also acute diarrhea is one of the major causes of morbidity and mortality among children less than 5 years of age.

Methods: In our study, fecal samples (n = 130) were collected from children (<5 years) presenting with symptoms of acute diarrhea. Samples were screened for viral, bacterial, and parasitic etiologies. Rotavirus and Adenovirus were screened by immunochromatographic tests. Diarrheagenic Escherichia coli (EPEC, EHEC, STEC, EAEC, O157, O111), Shigella spp., Salmonella spp., Vibrio cholera, Cryptosporidium spp., and Giardia spp. were detected by gene-specific polymerase chain reaction.

Results: Escherichia coli was detected to be the major etiological agent (30.07%) followed by Rotavirus (26.15%), Shigella (23.84%), Adenovirus (4.61%), Cryptosporidium (3.07%), and Giardia (0.77%). Concurrent infections with two or more pathogens were observed in 44 of 130 (33.84%) cases with a predominant incidence particularly in <2-year-old children (65.90%) compared to children of 2–5 years age group (34.09%). An overall result showed significantly higher detection rates among children with diarrhea in both combinations of two as well as three infections concurrently (p = 0.004915 and 0.03917, respectively).

Conclusion: Suspecting possible multiple infectious etiologies and diagnosis of the right causative agent(s) can aid in a better pharmacological management of acute childhood diarrhea. It is hypothesized that in cases with concurrent infections the etiological agents might be complementing each other’s strategies of pathogenesis resulting in severe diarrhea that could be studied better in experimental infections.

Keywords: Diarrhea, Infectious diarrhea, Children, Concurrent infection, Co-infection, Odisha.
In silico identification and validation of a novel hypothetical protein in Cryptosporidium hominis and virtual screening of inhibitors as therapeutics

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Abstract

Computational approaches to predict structure/function and other biological characteristics of proteins are becoming more common in comparison to the traditional methods in drug discovery. Cryptosporidiosis is a major zoonotic diarrheal disease particularly in children, which is caused primarily by Cryptosporidium hominis and Cryptosporidium parvum. Currently, there are no vaccines for cryptosporidiosis and recommended drugs are ineffective. With the availability of complete genome sequence of C. hominis, new targets have been recognized for the development of effective and better drugs and/or vaccines. We identified a unique hypothetical protein (TU502HP) in the C. hominis genome from the CryptoDB database. A three-dimensional model of the protein was generated using the Iterative Threading ASSEmbly Refinement server through an iterative threading method. Functional annotation and phylogenetic study of TU502HP protein revealed similarity with human transportin 3. The model is further subjected to a virtual screening study form the ZINC database compound library using the Dock Blaster server. A docking study through AutoDock software reported N(3chlorobenzyl)ethane1,2diamine as the best inhibitor in terms of docking score and binding energy. The reliability of the binding mode of the inhibitor is confirmed by a complex molecular dynamics simulation study using GROMACS software for 10 ns in the water environment. Furthermore, antigenic determinants of the protein were determined with the help of DNASTAR software. Our findings report a great potential in order to provide insights in the development of new drug(s) or vaccine(s) for treatment and prophylaxis of cryptosporidiosis among humans and animals.

Keywords: C. hominis, Hypothetical protein, Molecular docking, Molecular dynamics simulation.
Revisiting the global problem of cryptosporidiosis and recommendations

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Abstract
Cryptosporidiosis is a gastrointestinal illness caused by the protozoan parasite Cryptosporidium species, which is a leading cause of diarrhea in a variety of vertebrate hosts. The primary mode of transmission is through oral routes; infections spread with the ingestion of oocysts by susceptible animals or humans. In humans, Cryptosporidium infections are commonly found in children and immunocompromised individuals. The small intestine is the most common primary site of infection in humans while extraintestinal cryptosporidiosis occurs in immunocompromised individuals affecting the biliary tract, lungs, or pancreas. Both innate and adaptive immune responses play a critical role in parasite clearance as evident from studies with experimental infection in mice. However, the cellular immune responses induced during human infections are poorly understood. In this article, we review the currently available information with regard to epidemiology, diagnosis, therapeutic interventions, and strategies being used to control cryptosporidiosis infection. Since cryptosporidiosis may spread through zoonotic mode, we emphasize on more epidemiological surveillance-based studies in developing countries with poor sanitation and hygiene. These epidemiological surveys must incorporate fecal source tracking measures to identify animal and human populations contributing significantly to the fecal burden in the community, as mitigation measures differ by host type.

Keywords: Cryptosporidiosis, Cryptosporidium, diarrhea, microbial source tracking, zoonotic diseases.
Second-hand smoke knowledge and exposure among adults in rural Pedas, Negeri Sembilan

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Abstract

Background: It is an undeniable fact that exposure to tobacco smoke from the ambiance poses harmful effects to human health. Although many countries including Malaysia have imposed smoking bans and restrictions in indoor and outdoor public places, yet, to achieve a zero exposure to tobacco smoke from one’s surroundings remains a challenge.

Objective: The objectives of this study were to determine the second-hand smoke (SHS) knowledge and percentage of exposure among adults of rural Pedas, Negeri Sembilan and assess the association between socio-demographics and knowledge of SHS among these adults.

Methods: A cross sectional study with convenient sampling was carried out on 485 adults in Pedas, Negeri Sembilan. The instrument used was a validated questionnaire which was adapted with permission to suit the sample under study. The data collected were analysed with SPSS Statistics for Windows, Version 24.0.

Results: The percentage of SHS exposure among the non-smoking adults in rural Pedas, Negeri Sembilan was high (95.5%). More than 30% of the non-smoking respondents reported a daily exposure to SHS. The adults from this study however have good knowledge of SHS effects on health. A Mann-Whitney U test result revealed that knowledge on SHS scores was significantly higher for the non-smokers than that of smokers (U=17645, p < .001, r=.18). The top three locations identified as the most common places for SHS exposure were restaurants (38.9%), followed by workplace (26.2%) and home (19.4%).

Conclusions: The percentage of SHS exposure among the non-smoking adults of rural Pedas, Negeri Sembilan is high. Although the adults in this study have good knowledge of SHS health consequences, yet they are unavoidably exposed to SHS because smoking still occurs within their home, workplaces and public places. Our findings suggest the need for more comprehensive, assertive and strongly enforced policies to ban smoking in public areas, not only in this community but all across Malaysia.

Keywords: passive smoking, smoke exposure, awareness, adults, rural area.
Breast cancer is marked as one of the leading causes of malignancy-related morbidities worldwide. In spite of aggressive interventions, the inevitability of relapse and metastasis severely impede survival rates. Mounting evidence highlight the insidious role of cancer stem cells (CSCs), a small but significant subpopulation of undifferentiated cells that drive tumour progression, spread and resistance to conventional therapy. The nature and significance of breast CSCs remains poorly understood, and even disputed by many researchers. This review discusses the origins, biomarkers, signalling pathways, regulatory mechanisms, and targeted therapy of breast CSCs.

**Keywords:** Breast cancer stem cells (BCSCs), origins, biomarkers, signalling pathways, microRNAs, regulatory mechanisms, targeted therapy.
Development and validation of UV-spectrophotometric method for the estimation of curcumin in standardised polyherbal formulations

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Abstract

Objective: We aimed to develop and validate a simple UV-spectrophotometric method relates to the estimation of curcumin in standardised polyherbal formulations.

Methods: Pure curcumin was received as generous gift sample from Andhra University, India, all solvents and reagents of analytical reagent (AR) grade were procured from local suppliers and readily used for the method development. The method validation parameters were evaluated as per International Conference on Harmonization (ICH) guidelines. Further, this method was applied for the assay of curcumin in marketed product Live-well™, CUMIN (standardised turmeric extract (STE) fortified with standardised black pepper (SBE) extract) capsules using UV-spectrophotometric method.

Results and Discussion: It was confirmed from the results of method validation characteristics such as specificity, linearity, range, precision, accuracy, and robustness were keeping within the limits of acceptance criteria defined under ICH guidelines, 76.0560% of curcumin was estimated to be present in each Live-well™, CUMIN capsule containing a minimum 95% of the total curcuminoids (label claimed).

Conclusion: In summary, our method was found to be reliable in detecting the unknown percentage of curcumin in Live-well™, CUMIN capsule formulation. Also, the method was proved to be specific, linear, precise, accurate and robust to use for routine analysis of polyherbal formulations containing curcumin as their principal component in the extracts.

Keywords: UV-spectrophotometric method, Curcumin, ICH Guidelines, Live-well™, CUMIN.

Characterisation of ionic liquids nanoemulsion loaded with piroxicam for drug delivery system

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Abstract

In this study, ionic liquid-in-oil nanoemulsion (IL/o NEs) system were formulated by using two types of ionic liquids, 1-hexyl-3-methylimidazolium chloride [Hmim][Cl] and 1-butyl-3-methylimidazolium hexafluorophosphate [Bmim][PF6] in differences mass ratio with Tween-80/Span-20 1:1, 1:2, 2:1 and 2:3. They were tested for stability study before undergo characterisation, rheology behaviour and released study in order to get the best result of NE system. The high concentration of Tween-80 in the formulation of NEs shows high stability from separation, creaming, sedimentation and flocculation. The droplet sizes, zeta potential, drug encapsulation efficiency (%) and pH value for all formulations were considered in the range of 100 to 500 nm, -37.3 to -55.3 mV, 60.02% to 98.76% and 4.72 to 5.50 respectively. Spherical droplets were seen in the transmission electron microscopy (TEM) images of the nanoemulsions. Rheological studies showed non-Newtonian shear thinning behaviour at low shear rate up to 14 S⁻¹ of NE for both ionic liquids. Nanoemulsions insertion of Piroxicam was used to investigate the in vitro drug releases via dialysis bag method. The permeation of drug demonstrated the optimized surfactant ratio is 2:1 and ionic liquid is [Hmim][Cl] with 93% of drug released. It is concluded that the NEs prepared from ionic liquids offered a good potential as a carrier for drug delivery of Piroxicam.

Keywords: Nanoemulsions, 1-Hexyl-3-methylimidazolium chloride, 1-Butyl-3-methylimidazolium, hexafluorophosphate, Piroxicam.
Management of thyrotoxicosis with atrial fibrillation - A case report

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Abstract

Background: Thyrotoxicosis is a condition occurs when excessive thyroid hormone level produced by overactive thyroid gland. It is the risk factor of getting atrial fibrillation (AF) as it could exert marked influences on electrical impulse generation and conduction which associated with shortening of action potential duration and contribute to AF.

Case: A 57 years old Chinese female was diagnosed with thyrotoxicosis and atrial fibrillation when she was admitted to emergency department of hospital with complaints of shortness of breath, dyskinesia, on and off palpitation, fine tremor, tachycardia, warm skin, firm, enlarged and palpable thyroid, having patches of vitiligo on hands and feet and increase bowel movement. The CT scan has revealed small infarct near left band ganglia.

Aims: The aims of management in this case were to resolve the symptoms presented and get the thyroid hormone levels restored to euthyroid state.

Results: Aspirin and propranolol were given immediately after diagnosis for symptomatic relieve and rate control. Carbimazole and dexamethasone were given concurrently for hyperthyroid management. Aspirin was then replaced by warfarin before patient discharged to have better control and reduce risk of stroke. Furthermore, the patient's ECG and INR were monitored closely for stroke prevention.

Keywords: Antithyroid drugs, Atrial fibrillation, Hyperthyroidism, Stroke prevention, Thyrotoxicosis.
A comparison of plain radiography with computer tomography in determining coronal and sagittal alignments following total knee arthroplasty

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Abstract

Introduction: Optimal coronal and sagittal component positioning is important in achieving a successful outcome following total knee arthroplasty (TKA). Modalities to determine postoperative alignment include plain radiography and computer tomography (CT) imaging. This study aims to determine the accuracy and reliability of plain radiographs in measuring coronal and sagittal alignment following TKA.

Materials and Methods: A prospective, consecutive study of 58 patients undergoing TKA was performed comparing alignment data from plain radiographs and CT imaging. Hip-knee-angle (HKA), sagittal femoral angle (SFA) and sagittal tibial angle (STA) measurements were taken by two observers from plain radiographs and compared with CT alignment. Intra- and inter-observer correlation was calculated for each measurement.

Results: Intra-observer correlation was excellent for HKA (r>0.89) with a mean difference of <1.9°. The least intraobserver correlation was better for SFA (mean r=0.58) with a mean difference of 8°. Inter-observer correlation was better for HKA (r>0.95) and STA (r>0.8) compared to SFA (r=0.5). When comparing modalities (radiographs vs CT), HKA estimations for both observers showed the least maximum and mean differences while SFA observations were the least accurate.

Conclusion: Radiographic estimation of HKA showed excellent intra- and inter-observer correlation and corresponds well with CT imaging. However, radiographic estimation of sagittal plane alignment was less reliably measured and correlated less with CT imaging. Plain biplanar prosthetic alignment following TKA.

Keywords: radiographs, computer tomography, coronal alignment, sagittal alignment, total knee arthroplasty.

**Do statins adversely affect the HbA1c of diabetic patients?**

Son WD, Teng CL.

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**Abstract**

This paper discusses the adverse effect of statins on the HbA1c levels of diabetic patients. Studies have shown that statins may slightly worsen the HbA1c level. The effects vary depending on the type of statins, the dosage and the duration of therapy. However, it has been confirmed that statin use has benefits that outweigh its harms. Therefore, a diabetic patient should be given advice on the need for appropriate lifestyle changes and the importance of continuing the statins.
Cudraflavone C induces tumor-specific apoptosis in colorectal cancer cells through inhibition of the phosphoinositide 3-kinase (PI3K)-AKT pathway

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Abstract

Cudraflavone C (Cud C) is a naturally-occurring flavonol with reported anti-proliferative activities. However, the mechanisms by which Cud C induced cytotoxicity have yet to be fully elucidated. Here, we investigated the effects of Cud C on cell proliferation, caspase activation and apoptosis induction in colorectal cancer cells (CRC). We show that Cud C inhibits cell proliferation in KM12, Caco-2, HT29, HCC2998, HCT116 and SW48 CRC but not in the non-transformed colorectal epithelial cells, CCD CoN 841. Cud C induces tumor-selective apoptosis via mitochondrial depolarization and activation of the intrinsic caspase pathway. Gene expression profiling by microarray analyses revealed that tumor suppressor genes EGR1, HUWE1 and SMG1 were significantly up-regulated while oncogenes such as MYB1, CCNB1 and GPX2 were down-regulated following treatment with Cud C. Further analyses using Connectivity Map revealed that Cud C induced a gene signature highly similar to that of protein synthesis inhibitors and phosphoinositide 3-kinase (PI3K)-AKT inhibitors, suggesting that Cud C might inhibit PI3K-AKT signaling. A luminescent cell free PI3K lipid kinase assay revealed that Cud C significantly inhibited p110β/p85α PI3K activity, followed by p120γ, p110δ/p85α, and p110α/p85α PI3K activities. The inhibition by Cud C on p110β/p85α PI3K activity was comparable to LY-294002, a known PI3K inhibitor. Cud C also inhibited phosphorylation of AKT independent of NFκB activity in CRC cells, while ectopic expression of myristoylated AKT completely abrogated the anti-proliferative effects, and apoptosis induced by Cud C in CRC. These findings demonstrate that Cud C induces tumor-selective cytotoxicity by targeting the PI3K-AKT pathway. These findings provide novel insights into the mechanism of action of Cud C, and indicate that Cud C further development of Cud C derivatives as potential therapeutic agents is warranted.
Slow progress in diarrhea case management in low and middle income countries: Evidence from cross-sectional national surveys, 1985–2012

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Abstract

Background: Diarrhea remains to be a main cause of childhood mortality. Diarrhea case management indicators reflect the effectiveness of child survival interventions. We aimed to assess time trends and country-wise changes in diarrhea case management indicators among under-5 children in low-and-middle-income countries.

Methods: We analyzed aggregate data from Demographic and Health Surveys and Multiple Indicator Cluster Surveys done from 1986 to 2012 in low-and-middle-income countries. Two-week prevalence rates of diarrhea, caregiver's care seeking behavior and three case management indicators were analyzed. We assessed overall time trends across the countries using panel data analyses and country-level changes between two sequential surveys.

Results: Overall, yearly increase in case management indicators ranged from 1 · 3 to 2 · 5%. In the year 2012, <50% of the children were given correct treatment (received oral rehydration and increased fluids) for diarrhea. Annually, an estimated 300 to 350 million children were not given oral rehydration solutions, or recommended home fluids or ‘increased fluids’ and 304 million children not taken to a healthcare provider during an episode of diarrhea. Overall, care seeking for diarrhea, increased from pre-2000 to post-2000, i.e. from 35 to 45%; oral rehydration rates increased by about 7% but the rate of ‘increased fluids’ decreased by 14%. Country-level trends showed that care seeking had decreased in 15 countries but increased in 33 countries. Care seeking from a healthcare provider increased by ≥10% in about 23 countries. Oral rehydration rates had increased by ≥10% in 15 countries and in 30 countries oral rehydration rates increased by <10%.

Conclusions: Very limited progress has been made in the case management of childhood diarrhea. A better understanding of caregiver’s care seeking behavior and health care provider’s case management practices is needed to improve diarrhea case management in low- and-middle-income countries.

Keywords: Under-5 child, Diarrhea, Oral rehydration therapy, Case management, Child health services, Developing countries, Trends.

Association of adult tobacco use with household food access insecurity: Results from Nepal demographic and health survey, 2011

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Abstract

Background: Food insecurity is a very common problem in developing countries particularly among the poorer households. Very few studies have tested the association between adult smoking and food insecurity.

Methods: We analysed the data from a nationally representative sample of 10,826 households in which women and men (in a sub sample of 4121 households) aged 15-49 years were interviewed in Nepal Demographic and Health Survey 2011. Data from households in which both men and women were interviewed were analysed for association of household food insecurity access score (HFIAS), with tobacco use among men and women, sociodemographic and spatial factors. Univariate comparisons followed by zero-inflated negative binomial regression analyses were done to determine the association between HFIAS and individual, household and spatial factors.

Results: Mean HFIAS score was 3.5 (SD, 4.6) whereas the median was 0 (IQR 0-6). Prevalence of tobacco use among men and women was 50.2% (95% CIs 47.9, 52.6), and 17.3% (95% CIs 15.7, 18.9). HFIAS scores were significantly higher among households where men used tobacco (4.96), and men either smoked or use SLT (3.82) as compared to those without tobacco users (2.79). HFIAS scores were not significantly different by tobacco use status of women. HFIAS score was highest in the poorest households and vice versa. After adjusting for covariates association between HFIAS score and male tobacco use remained significant but effect size decreased when covariates were included into regression models (adjusted OR 1.11). HFIAS score was also associated wealth index (adjusted OR 0.86-0.62) and ecological region (adjusted OR 1.33) and development regions (adjusted OR 1.10-1.21).

Conclusion: Tobacco users in poor(er) households should be encouraged to ‘quit’ their habit. Less affluent sectors of the population also need to be educated about the non-health benefits of quitting, such as improved economic status and reduced food insecurity.

Keywords: Food insecurity, Nepal, Poverty, Tobacco use, Smoking.
Milk vitamin D in relation to the ‘adequate intake’ for 0–6-month-old infants: A study in lactating women with different cultural backgrounds, living at different latitudes

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Abstract
Breast-fed infants are susceptible to vitamin D deficiency rickets. The current vitamin D ‘adequate intake’ (AI) for 0-6-month-old infants is 10 µg/d, corresponding with a human milk antirachitic activity (ARA) of 513 IU/l. We were particularly interested to see whether milk ARA of mothers with lifetime abundant sunlight exposure reaches the AI. We measured milk ARA of lactating mothers with different cultural backgrounds, living at different latitudes. Mature milk was derived from 181 lactating women in the Netherlands, Curaçao, Vietnam, Malaysia and Tanzania. Milk ARA and plasma 25(OH)D were analysed by liquid-chromatography-MS/MS; milk fatty acids were analysed by GC-flame ionisation detector (FID).

None of the mothers reached the milk vitamin D AI. Milk ARA (n; median; range) were as follows: Netherlands (n 9; 46 IU/l; 3-51), Curaçao (n 10; 31 IU/l; 5-113), Vietnam: Halong Bay (n 20; 58 IU/l; 23-110), Phu Tho (n 22; 28 IU/l; 1-62), Tien Giang (n 20; 63 IU/l; 26-247), Ho-Chi-Minh-City (n 18; 49 IU/l; 24-116), Hanoi (n 21; 37 IU/l; 11-118), Malaysia-Kuala Lumpur (n 20; 14 IU/l; 1-46) and Tanzania-Ukerewe (n 21; 77 IU/l; 12-232) and Maasai (n 20; 88 IU/l; 43-189). We collected blood samples of these lactating women in Curaçao, Vietnam and from Tanzania-Ukerewe, and found that 33·3 % had plasma 25(OH)D levels between 80 and 249·9 nmol/l, 47·3 % between 50 and 79·9 nmol/l and 19·4 % between 25 and 49·9 nmol/l. Milk ARA correlated positively with maternal plasma 25(OH)D (range 27-132 nmol/l, r 0·40) and milk EPA+DHA (0·1-3·1 g%, r 0·20), and negatively with latitude (2°S-53°N, r -0·21). Milk ARA of mothers with lifetime abundant sunlight exposure is not even close to the vitamin D AI for 0-6-month-old infants. Our data may point at the importance of adequate fetal vitamin D stores.

Keywords: 25(OH)D 25-hydroxyvitamin D, AI adequate intake, ARA antirachitic activity, DBP vitamin D binding protein, IOM Institute of Medicine, PP postpartum, Adequate intake, Antirachitic activity, Breast milk, Fish oil, Vitamin D.
Evaluation of workshop for training house-officers and medical officers on medical emergencies using simulation for workplace preparedness

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Abstract

Background: House-officers and medical officers are at the forefront during medical emergencies in the ward and casualty which impose cognitive, communication, social and system challenges and yet, training in this area is commonly lacking. A workshop was conducted using simulation to provide training on some acute medical emergencies like cord prolapse, post-partum haemorrhage with collapse, poly-trauma and acute exacerbation of asthma.

Objective: To determine the effectiveness of simulation in developing competency in managing selected clinical emergencies.

Methodology: There were 22 participants consisting of house-officers, junior medical officers and nursing clinical instructors. Only doctors were included in the study. Four medical emergencies were chosen viz.: Cord prolapse; post-partum haemorrhage with collapse; poly-trauma and acute exacerbation of asthma. The simulated sessions were conducted using high fidelity manikins and simulated patients. Simulated patients were trained and moulage was applied accordingly. The skills stations were on airway equipment and techniques of application, latest cardiac life support algorithm and hands on chest compression using manikins.

Results: A 5 point Likert scale used to rate the sessions. The skills station had 65% (n=13) rating as excellent and 35% (n=7) good. The skills simulation was rated excellent by 75% (n=15) and good by 25% (n=5) of participants. Verbal feedback was that it was very refreshing, informative, and helpful in terms of improving their skills.

Conclusion: The simulated skills training for the junior doctors was very well received and maybe beneficial for work preparedness and in the long run address patient safety.

Keywords: Junior doctors, medical emergencies, medical curriculum, resuscitation, simulation, work-preparedness.
Synthesis of some novel quinazoline derivatives having anti-cancer activity

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Abstract
Cancers are the leading causes of morbidity and mortality worldwide. There are an estimated 14.1 million new cases of cancer in the world and the childhood cancers represent a small fraction of total cancers with the estimated values of 150,000 diagnosis each year. Cancers are a large family of diseases that involve abnormal cell growth with the potential to invade or spread to other parts of the body. Hence, some new semi carbazides containing quinazoline moieties have been synthesized and their ability to inhibit growth of human cancer cell lines has been evaluated. The compound S1 and S3 has shown remarkable anticancer activity. The structures of all the compounds have been confirmed by FT-IR, NMR, and mass spectral analysis.

Keywords: Semicarbazides, Quinazoline, Anticancer activity, Cancer, Morbidity.
Tadiparthi K, Raghavendra S, Kamal A. A catalytic, one-pot and green synthesis of α-amino nitriles: Cu(BF4)2.xH2O an efficient catalyst. *Letters in Organic Chemistry*, 2017; 14(6): 440-445. (ISI IF: 0.73; CiteScore: 0.65; Tier: Q4).

**A Catalytic, One-pot and Green Synthesis of α-Amino Nitriles: Cu(BF4)2.x H2O an Efficient Catalyst**

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**Abstract**

**Background:** The Strecker reaction is a first reported multicomponent reaction for the preparation of α-amino nitriles. The α-amino nitriles are important intermediates for various amino acids, 1,2-diazines, heterocycles and biologically active compounds like Saframycin A and Ecteinascidin 746. The preparation of α-amino nitriles by Strecker approach using MCR attracted many research groups owing atom economy to avoid multistep synthesis and to follow Green chemistry principles.

**Methods:** α-amino nitriles have been synthesized using Strecker reaction by treatment of aldehydes, amines, with TMSCN in the presence of Cu(BF4)2.xH2O as a catalyst in one pot under neat conditions. Various aromatic and aliphatic aldehydes have been studied with different primary and secondary amines.

**Results:** The reaction condition has been optimized by choosing a model reaction under various solvents and found good yields under neat conditions. Moreover, various catalytic amounts of Cu(BF4)2.xH2O has also been studied and found 3 mole% providing better yields. The reaction has been studied with different substrates of aldehydes and amines. Some of the products were characterized by comparison of their spectral data (1H NMR, 13C NMR, IR and MS) and physical properties with those of authentic samples reported in the literature.

**Conclusion:** A facile and efficient one-pot synthesis of α-amino nitriles at ambient temperature using copper(II)tetrafluoroborate as a novel catalyst under solvent-free conditions via Strecker reaction is reported. The process is simple and environmentally benign using the commercially available and inexpensive catalyst.

**Keywords:** α-Amino nitriles, copper(II)tetrafluoroborate, green chemistry, one-pot synthesis, solvent free, Strecker synthesis.
Tan BH, Pan Y, Dong AN, Ong CE. In vitro and in silico approaches to study cytochrome P450-mediated interactions. *Journal of Pharmacy and Pharmaceutical Sciences*, 2017; 20: 319-28. (ISI IF: 1.811; CiteScore: 2.18; Tire: Q2).

**In vitro and in silico approaches to study cytochrome P450-mediated interactions**

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**Abstract**

*In vitro* and *in silico* models of drug metabolism are utilized regularly in the drug research and development as tools for assessing pharmacokinetic variability and drug-drug interaction risk. The use of *in vitro* and *in silico* predictive approaches offers advantages including guiding rational design of clinical drug-drug interaction studies, minimization of human risk in the clinical trials, as well as cost and time savings due to lesser attrition during compound development process. This article gives a review of some of the current *in vitro* and *in silico* methods used to characterize cytochrome P450(CYP)-mediated drug metabolism for estimating pharmacokinetic variability and the magnitude of drug-drug interactions. Examples demonstrating the predictive applicability of specific *in vitro* and *in silico* approaches are described. Commonly encountered confounding factors and sources of bias and error in these approaches are presented. With the advent of technological advancement in high throughput screening and computer power, the *in vitro* and *in silico* methods are becoming more efficient and reliable and will continue to contribute to the process of drug discovery, development and ultimately safer and more effective pharmacotherapy.
Influence of geographical origins on the physicochemical properties of hass avocado oil

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Abstract

A study was conducted to compare the physicochemical properties of Hass avocado oil from different geographical locations (Mexico, Australia, United States and New Zealand). Regardless of geographical origins, Hass avocado pulp was characterized by high lipid content (61.27–62.66%). Among Hass avocados of different origins examined, avocado oil of New Zealand origin exhibited the lowest saponification value. The $L^*$, $a^*$ and $b^*$ values for avocados of New Zealand origin were higher than others, translating into the oil being the lightest in color and containing more red and yellow pigments. The predominant fatty acids in the Hass avocado oil were oleic (42.59–50.97%) and palmitic (20.61–25.63%) acids, whereas the predominant triacylglycerols (TAGs) were OOO (21.41–34.69%) and POO (19.65–24.68%), where O and P denote oleic and palmitic acids, respectively. The melting curves of Hass avocado oil displayed three endothermic peaks, whereas the crystallization curves displayed two endothermic peaks. Hass avocado oil of New Zealand origin contained a significant amount of natural pigments and unsaturated compounds (unsaturated fatty acids and tri-unsaturated TAGs) than Mexico, Australia and United States origins.

Keywords: Hass avocado oil, Physicochemical properties, Geographical origin.

Tumor regression and modulation of gene expression via tumor-targeted tocotrienol niosomes

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Abstract

**Aim:** To develop 6-O-palmitoyl-ascorbic acid-based niosomes targeted to transferrin receptor for intravenous administration of tocotrienols (T3) in breast cancer.

**Materials and Methods:** Niosomes were prepared using film hydration and ultrasonication methods. Transferrin was coupled to the surface of niosomes via chemical linker. Nanovesicles were characterized for size, zeta potential, morphology, stability and biological efficacy.

**Results:** When evaluated in MDA-MB-231 cells, entrapment of T3 in niosomes caused 1.5-fold reduction in IC₅₀ value compared with nonformulated T3. In vivo, the average tumor volume of mice treated with tumor-targeted niosomes was 12-fold lower than that of untreated group, accompanied by marked downregulation of three genes involved in metastasis.

**Conclusion:** Findings suggested that tumor-targeted niosomes served as promising delivery system for T3 in cancer therapy.

**Keywords:** 6-O-palmitoyl-ascorbic acid, active targeting, breast cancer, niosomes, tocotrienols, transferrin.
Tan OH, Tan EHP, Ooi IH. Fast gradient normal-phase high pressure liquid chromatography for rapid baseline separation of nine vitamin E homologues in palm tocotrienol rich fraction (TRF). RSC-Analytical Methods, 2017; 9(35): 5211-5218. DOI: 10.1039/C7AY00924K. (ISI IF: 1.9; CiteScore: 1.99; Tier: Q1).

Fast gradient normal-phase high pressure liquid chromatography for rapid baseline separation of nine vitamin E homologues in palm tocotrienol rich fraction (TRF)

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Abstract
A rapid, accurate and precise normal phase high pressure liquid chromatographic method was developed and validated for the simultaneous determination of nine vitamin E forms comprised of \( \alpha \)-tocomonoenol, \( \alpha \)-, \( \beta \)-, \( \gamma \)-, and \( \delta \)-tocopherols and \( \alpha \)-, \( \beta \)-, \( \gamma \)-, and \( \delta \)-tocotrienols in tocotrienol rich fractions (TRFs) derived from palm oil. The chromatographic separation of vitamin E was performed on a silica HPLC column thermostated at 40 °C using n-heptane and ethyl acetate as the mobile phase in a gradient elution mode. The calibration standard curves were linear over the concentration range from 0.1 to 1.0 mg mL for all vitamin E forms with overall R > 0.9980. The percent relative standard deviation of the method repeatability was less than 2.0% and the recovery ranged between 90 and 110%. The instrument limit of detection and quantitation ranged from 0.04 to 0.05 mg mL and from 0.11 to 0.18 mg mL respectively. The separation was completed in 15 minutes with an additional 2 minutes for re-equilibration. In conclusion, a method has been successfully developed and validated for the simultaneous analysis of nine vitamin E forms in palm oil which is suitable for routine quality control of all vitamin E forms in palm TRFs at different compositions.

**Pteropine orthoreovirus: An important emerging virus causing infectious disease in the tropics?**

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**Abstract**

**Introduction:** *Pteropine orthoreovirus* (PRV) is an emerging zoonotic respiratory virus that has spilled over from bats to humans. Though initially found only in bats, further case studies have found viable virus in ill patients.

**Methodology:** PubMed was queried with the keywords of *Nelson Bay orthoreovirus* OR *Pteropine orthoreovirus* OR *Melaka orthoreovirus* OR *Kampar orthoreovirus*, and returned 17 hits.

**Results:** Based on prevalence studies, the presence of PRV has been reported in Malaysia and Vietnam, both developing countries. Other case reports also provide further evidence of the presence of PRV in the Southeast Asian region. Despite the absence of PRV in their home countries, travellers from Hong Kong and Japan to Indonesia have returned to their countries ill with this virus, indicating that local communities in Indonesia might be affected by this virus.

**Conclusions:** This work aims to bring to light this emerging zoonotic respiratory virus circulating among developing countries in Southeast Asia. To improve the understanding of PRV of the medical and scientific community in the Southeast Asian region, this work introduces the general features of PRV, reports of imported PRV, prevalence, and clinical features of PRV. Gaps in knowledge about PRV have also been identified in this work, and we hope that future studies can be undertaken to improve our understanding of this virus.

**Key words:** *Pteropine orthoreovirus*, Melaka virus, Nelson Bay virus, Kampar virus, Pulau virus.

**Registered nurses’ attitude towards physician-nurse collaboration in a Malaysian private hospital**

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**Abstract**

**Background:** Positive physician-nurse collaborative relationship is the key determinant for patients’ outcomes.

**Objective:** The purpose of the study was to investigate registered nurses’ attitude towards physician-nurse collaboration and its association with demographic characteristics.

**Methodology:** The study was descriptive and cross-sectional. The data of the study was collected using the “Jefferson Scale of Attitudes toward Physician-Nurse Collaboration”. The sample size of the study was 127 registered nurses recruited using convenience sampling. Descriptive statistics and inferential statistics t-test were used for data analysis.

**Results:** The results showed that nurses’ attitude towards physician-nurse collaboration was positive ($M$=3.25, $SD$±0.29). The attitude of the participants was highly positive towards “shares education and collaboration” ($M$=3.42, $SD$±0.36), “nurse’s autonomy” ($M$=3.42, $SD$±0.44), and “caring vs. curing” subscales ($M$=3.41, $SD$±0.41). However, the participants rated lowest for “physician's authority” subscale ($M$=2.12, $SD$±0.83) and particularly on the item “doctors should be dominant authority in all health care matters” ($M$=2.11, $SD$±0.99). Furthermore, t-test analysis revealed no significant association between nurses’ attitude towards physician-nurse collaboration and demographic characteristics such as age, gender, and educational level ($p > 0.05$).

**Conclusion:** The results of the study provided some crucial evidences on nurses’ attitude towards physician-nurse collaboration. The evidences are useful for the relevant stakeholders to initiate relevant strategies to improve and strengthen the relationship gap between physicians and nurses.

**Keywords:** Attitude, physician-nurse, collaboration, registered nurses.
Teo CHJ, Lim PKC, Voon K, Mak JW. Detection of dengue viruses and Wolbachia in Aedes aegypti and Aedes albopictus larvae from four urban localities in Kuala Lumpur, Malaysia. Tropical Biomedicine, 2017; 34(3): 583–597. (CiteScore: 0.95; Tier: Q3).

Detection of dengue viruses and Wolbachia in Aedes aegypti and Aedes albopictus larvae from four urban localities in Kuala Lumpur, Malaysia

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Abstract

Dengue fever (DF) is currently one of the most important mosquito-borne diseases that affects humans. Dengue fever (DF) and dengue hemorrhagic fever (DHF) are caused by four serotypes of dengue viruses (DENV-1 to DENV-4). The main vector transmitting dengue is Aedes aegypti while Aedes albopictus acts as a secondary vector. As treatment is unavailable and the first dengue vaccine approved in Mexico, Dengvaxia® has yet to be accepted worldwide, prevention of the disease relies heavily on surveillance and control of mosquito vectors. A transgene driver, Wolbachia was found to limit the transmission of dengue virus in Aedes mosquitoes. Wolbachia alone was able to inhibit viral replication, dissemination and transmission in A. aegypti mosquitoes in experimental studies. In A. albopictus, Wolbachia did not affect the replication of dengue virus but was able to reduce the viral infection of mosquito salivary glands and limit transmission. Studies on Wolbachia have all been carried out in adult Aedes mosquitoes, hence this study was conducted to determine the presence of dengue virus serotypes and Wolbachia in A. aegypti and A. albopictus larvae collected from ovitraps in four localities in Kuala Lumpur viz. Happy Gardens, IMU Bukit Jalil, Ampang and Taman Yarl. Another objective of this study was to determine the association between dengue virus serotypes and the presence of Wolbachia in A. aegypti and A. albopictus larvae. A total of 300 mosquito larvae was collected; 99 (Happy Gardens), 85 (Bukit Jalil), 73 (Ampang) and 43 (Taman Yarl). Out of 300 larvae collected, 284 were identified as A. albopictus and 16 others were identified as A. aegypti. Of the 284 A. albopictus larvae collected, 211 (74.3%) and 73 (25.7%) were found to be negative and positive for dengue virus respectively. The dengue serotypes detected were 2 DENV-2 (2.7%), 58 DENV-3 (79.5%) and 13 DENV-4 (17.8%). DENV-1 was not detected in any of the A. albopictus larvae. For A. aegypti, out of 16 A. aegypti larvae collected, 12 (75%) were found to be negative and 4 (25%) were positive for DENV-2. For the detection of Wolbachia in A. albopictus, 71 out of 284 (25%) and 213 (75%) larvae were found to be positive and negative for Wolbachia respectively. For A. aegypti, 4 (25%) and 12 (75%) out of 16 larvae were positive and negative for Wolbachia respectively. This is the first report of Wolbachia in A. albopictus and A. aegypti larvae in Malaysia. A chisquare test analysis to determine the association between dengue virus and Wolbachia in A. albopictus and A. aegypti larvae collected from the four localities in Kuala Lumpur showed that there was no association ($\chi^2 = 3.080; df = 1; P > 0.05$).
Novel furan-containing peptide-based inhibitors of protein arginine deiminase type IV (PAD4)

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Abstract
Protein arginine deiminase type IV (PAD4) is responsible for the post-translational conversion of peptidylarginine to peptidylcitrulline. Citrullinated protein is the autoantigen in rheumatoid arthritis, and therefore, PAD4 is currently a promising therapeutic target for the disease. Recently, we reported the importance of the furan ring in the structure of PAD4 inhibitors. In this study, the furan ring was incorporated into peptides to act as the “warhead” of the inhibitors for PAD4. IC50 studies showed that the furan-containing peptide-based inhibitors were able to inhibit PAD4 to a better extent than the furan-containing small molecules that were previously reported. The best peptide-based inhibitor inhibited PAD4 reversibly and competitively with an IC50 value of 243.2 ± 2.4 μM. NMR spectroscopy and NMR-restrained molecular dynamic simulations revealed that the peptide-based inhibitor had a random structure. Molecular docking studies showed that the peptide-based inhibitor entered the binding site and interacted with the essential amino acids involved in the catalytic activity. The peptide-based inhibitor could be further developed into a therapeutic drug for rheumatoid arthritis.
In vitro evaluation of novel phenytoin-loaded alkyd nanoemulsions designed for application in topical wound healing

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Abstract
Phenytoin-loaded alkyd nanoemulsions were prepared spontaneously using the phase inversion method from a mixture of novel biosourced alkyds and Tween 80 surfactant. Exposure of human adult keratinocytes (HaCaT cells) for 48 h to alkyd nanoemulsions producing phenytoin concentrations of 3.125-200 mg/mL resulted in relative cell viability readings using tetrazolium dye 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide of 100% confirming nontoxicity and suggesting cell proliferation activity. Phenytoin-loaded alkyd nanoemulsions generally resulted in higher mean cell viability compared with equivalent concentration of phenytoin solutions, suggesting that the nanoemulsions provided a controlled-release property that maintained the optimum phenytoin level for keratinocyte growth. HaCaT cell proliferation, measured by 5-bromo-2-deoxyuridine uptake, was found to increase following exposure to increasing phenytoin concentration from 25 to 50 mg/mL in solution or encapsulated in nanoemulsions but declined at a drug concentration of 100 mg/mL. An in vitro cell monolayer wound scratch assay revealed that phenytoin solution or nanoemulsions producing 50 mg/mL phenytoin concentration resulted in 75%-82% “scratch closure” after 36 h, similar to medium containing 10% fetal bovine serum as a cell growth promoter. These findings indicate that phenytoin-loaded alkyd nanoemulsions show potential for promoting topical wound healing through enhanced proliferation of epidermal cells.

Keywords: alkyd nanoemulsion, phenytoin, topical, wound healing.
Pathogenic role of exosomes in Epstein-Barr virus (EBV)-associated cancers

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Abstract
Exosomes are 40- to 100-nm membrane-bound small vesicles that carry a great variety of cellular cargoes including proteins, DNA, messenger RNAs (mRNAs), and microRNAs (miRNAs). These nanovesicles are detected in various biological fluids such as serum, urine, saliva, and seminal fluids. Exosomes serve as key mediators in intercellular communication by facilitating the transfer and exchange of cellular components from cells to cells. They contain various pathogenic factors whereby their adverse effects have been implicated in multiple viral infections and cancers. Interestingly, accumulating evidences showed that exosomes derived from tumour viruses or oncoviruses, exacerbate virus-associated cancers by remodelling the tumour microenvironment. In this review, we summarize the contributing factors of Epstein-Barr virus (EBV) products-containing exosomes in viral pathogenesis and their potential implications in EBV-driven malignancies. Understanding the biological role of these exosomes in the disease would undoubtedly boost the development of a more comprehensive strategy to combat EBV-associated cancers and to better predict the therapeutic outcomes. Furthermore, we also highlight the potentials and challenges of EBV products-containing exosomes being employed as diagnostic markers and therapeutic targets for EBV-related cancers. Since these aspects are rather underexplored, we attempt to underline interesting areas that warrant further investigations in the future.

Keywords: Exosome, Epstein-Barr virus, EBV-associated cancer, LMP, nasopharyngeal carcinoma.
Prevalence of depressive disorder and its association with perceived social support among patients with human immunodeficiency virus (HIV) in Hospital Tuanku Ja’afar, Seremban (HTJS), Malaysia

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Abstract

Objectives: This study aimed to determine the prevalence of depressive disorder and its association with perceived social support among patients with HIV attending the Infectious Disease Clinic in HTJS.

Methods: A cross-sectional study was conducted, and systematic random sampling method was employed for the selection of participants. Socio-demographic and clinical details were obtained through a self-rated questionnaire and participants’ medical records. Depressive disorder was screened and diagnosed using the Mini International Neuropsychiatric Interview (M.I.N.I.) and perceived social support was determined using the Multidimensional Scale of Perceived Social Support (MSPSS). Appropriate statistical analyses were used to determine the prevalence of depressive disorder and its association with perceived social support.

Results: A total of 99 patients participated in this study. The mean age of participants was 38.16 ± 1.01 years, and the majority of participants were male (69.7%). Most of the participants were Malay (58.6%), followed by Indians (20.2%), Chinese (17.2%) and others (4.0%). The majority had completed secondary education (54%), and most were employed (79.8%). Most of the participants were single (45.5%) or married (45.5%). The lifetime and point prevalence of depressive disorder was 24.2% and 17.2%, respectively. About 64.7% of patients with depressive disorder were undiagnosed. Out of the 3 sources of perceived social support, perceived social support from a significant other (OR=0.53, p=0.042, CI=0.29, 0.98) and perceived social support from friends (OR=0.49, p=0.015, CI=0.27, 0.87) were found to be negative predictors for depressive disorder. Conclusion: This study reports that the prevalence disorder among patients with HIV in HTJS is higher than that of the general population. Patients without depressive disorder reported significantly higher perceived social support scores. Perceived social supports from significant others and friends were found to be important associated factors for lower depressive disorder vulnerability. Hence, physicians should routinely screen for depressive disorder in this vulnerable group and explore and mobilize their social support to reduce patients’ vulnerability to develop depressive disorder.

**Cervical pessary in the prevention of preterm births in multiple pregnancies with a short cervix: PRISMA compliant systematic review and meta-analysis**

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**Abstract**

**Background:** Preterm births occur frequently in multiple pregnancies with a short cervix. The cervical pessary is a potential intervention for prevention of preterm births.

**Objective:** To assess the effectiveness of cervical pessary in the prevention of preterm births in multiple pregnancies with a short cervix (<25 mm).

**Search strategy:** Major databases from 2006 to 20th November 2016 were searched for relevant terms.

**Selection criteria:** We included randomized controlled trials that assessed the effectiveness of cervical pessary on pregnancy outcomes in multiple pregnancies with a short cervix.

**Data collection and analysis:** Risk ratio was used as the summary measure with random effects model. We assessed heterogeneity between studies using the I index. Quality assessment was done based on Cochrane Handbook Method.

**Main results:** Pooled data showed no benefit of using cervical pessary in the prevention of preterm births, birth weights less than 1500 g, less than 2500 g, adverse neonatal events and fetal/neonatal deaths in twin pregnancies with a short cervix.

**Conclusion:** We are unable to show benefit of using cervical pessary in preventing preterm births in twin pregnancies with a short cervix. However, as cervical pessary is a reasonable intervention, there is a need for more randomized controlled trials in this area.

**Keywords:** Cervical pessary, preterm birth, multiple pregnancies, short cervix, systematic review.

Current attempts to implement microRNA-based diagnostics and therapy in cardiovascular and metabolic disease: a promising future

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Abstract

MicroRNAs (miRNAs) are small, noncoding RNAs regulating gene expression at the post-translational level. miRNA-based therapeutic agents are important because of the functionality of miRNAs in regulating lipid and glucose metabolism and their role in the pathogenesis of metabolic disorders such as diabetes and obesity, where dysregulation leads to disease; they are also important in angiogenesis. miRNAs additionally serve as biomarkers in the diagnosis, prognosis and risk assessment of disease and in monitoring the response to treatment. Here, we provide a brief overview of progress in miRNA-based therapeutics in the preclinical and clinical setting and highlight the novel outcomes and opportunities in the diagnosis and treatment of metabolic conditions. In addition, we present the role of miRNAs in stem cell therapy which could have great potential in regenerative medicine.

**Optimizing medication use among older people residing in aged care facilities**

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**Abstract**

Medication reviews are essential in the optimization of pharmacotherapy among the older population. This study developed a comprehensive approach to medication management among older people in aged care facilities. The framework is centered on medication appropriateness and comprises a five-step medication review algorithm that is supplemented with a 10-component tool, the Medication Appropriateness Index-Geriatric version (MAI-G). This version incorporates geriatric components and detects changes in medication use. The MAI-G supplements the algorithm and quantifies the appropriateness of medications, determining improvements and permitting measurable outcomes. The components in the MAI-G closely correspond to components in the algorithm to allow for quick and unequivocal extrapolation. The algorithm and MAI-G were implemented in a 6-month prospective study among 202 residents aged 60 years and above across 17 aged care facilities in Malaysia. The proportion of residents with inappropriate medications detected by the MAI-G were 55.0% at baseline, 50.5% at 3-months and 46.5% at 6-months. The number of inappropriate medications detected by the MAI-G also decreased from 0.83 ± 0.93 at baseline, to 0.76 ± 0.92 at 6-months. The MAI-G average scores decreased from 1.19 ± 1.03, at baseline, to 1.16 ± 0.98, at 6-months (MAI-G scores range from 0–21). This study supports the need for a comprehensive medication review process that is supplemented by quantification of medication appropriateness which identifies changes in medication use. This study also provides an overview of the medication appropriateness among older people residing in aged care facilities in Malaysia.
The chaperone in a medical examination and therapeutic relationship: A literature review and critical discussion

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Abstract

Background: A chaperone is encouraged to be present in any medical consultation especially when an intimate examination is required. This impartial attendant could be reassuring to the patient especially when gender is an issue and may avoid conflicts in the patient-physician relationship. Situations in which a chaperone is not available or is declined by the patient present special ethical problems and may impinge on an appropriate therapeutic relationship.

Objectives: The purpose of this study was to explore the issues involved in the engagement of chaperones in medical examinations in various countries and their implications concerning ethics and appropriate therapeutic relationships.

Method: A review of the medical literature in English between 1990 and 2016 was conducted. Data bases included PubMed, Cochrane Library, EBSCO Host, and Google Scholar. Search terms included “ethics”, “chaperone”, “patient-physician relationship” and “patient autonomy”. Additionally, medical ethics codes of various countries were considered. Grounded Theory methodology was employed for qualitative data analysis.

Results and Discussion: Through the indicated analyses, common themes and five main questions were elicited. They follow: 1) What are the duties of physicians when the patient declines having a chaperone during an intimate medical examination, 2) Do perceptions on the need for a chaperone differ according to physicians’ gender?, 3) What are patients’ perceptions on the presence of a chaperone?, 4) Can a physician refuse to see a patient?, and 5) Can the sexual orientation of the examining doctor or patient be always assumed?. The findings obtained are complemented with a critical discussion on ethics and therapeutic implications.

Conclusions: Having clear guidelines for intimate medical examinations provides the physician sound defence concerning allegations of misconduct and lends security and transparency to patients. Trust should remain the cornerstone of any therapeutic relationship. Medicolegal recommendations and standards of practice should be aligned with patient values and societal expectations. Good role modelling and teaching of professionalism in medical education years are important towards ethical practice of medicine.
**Keywords:** Ethics, chaperone, patient-doctor relationship, patient autonomy, person centered medicine.

**Narrative Medicine: An unexplored perspective in the medical curriculum to enhance patient-centredness and empathy in medical students**

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**Abstract**

A medical narrative is a physician-patient dialogue, where the physician listens carefully to fragments of the patient’s story, while interpreting their hidden messages and word sequences, as well as observing their gestures and body language. This aspect of the therapeutic relationship contributes to deciphering symptoms which are not apparent in the conventional interview and contributes to a much broader perspective of illness and health.

The arts and the humanities have always been inseparable from each other in medical education. In this biomedical revolution, the humanities are needed now more than ever before to bridge the divides that separate the physician from the patient, from self, from colleagues, and society.

Narrative Medicine (NM) which aims to treat the whole person, and not just the illness, is an emerging patient-centred discipline in medical schools that can humanise medical care and promote empathy.

NM helps medical students cope with the suffering of their patients as well as their own emotions by reducing the anxiety and threat that come with illness, thereby providing a psychologically-sound foundation for the development of self-reflection and empathy. NM facilitates medical students’ adoption of patients’ perspectives with the hope of ultimately leading to more humane, ethical and empathetic healthcare for their patients. The discipline of NM is critically examined in this review paper from the perspective of external and internal stakeholders.

**Keywords:** Narrative medicine, curriculum, patient-centredness, empathy, medical students.
Abstract

**Background:** Since 2000, the widespread adoption of pneumococcal conjugate vaccines (PCVs) has had a major impact in the prevention of pneumonia. Limited access to international financial support means some middle-income countries (MICs) are trailing in the widespread use of PCVs. We review the status of PCV implementation, and discuss any needs and gaps related to low levels of PCV implementation in MICs, with analysis of possible solutions to strengthen the PCV implementation process in MICs.

**Main body:** We searched PubMed, PubMed Central, Ovid MEDLINE, and SCOPUS databases using search terms related to pneumococcal immunization, governmental health policy or programmes, and MICs. Two authors independently reviewed the full text of the references, which were assessed for eligibility using pre-defined inclusion and exclusion criteria. The search terms identified 1,165 articles and the full texts of 21 were assessed for suitability, with eight articles included in the systematic review. MICs are implementing PCVs at a slower rate than donor-funded low-income countries and wealthier developed countries. A significant difference in the uptake of PCV in lower middle-income countries (LMICs) (71%) and upper middle-income countries (UMICs) (48%) is largely due to an unsuccessful process of “graduation” of MICs from GAVI assistance, an issue that arises as countries cross the income eligibility threshold and are no longer eligible to receive the same levels of financial assistance. A lack of country-specific data on disease burden, a lack of local expertise in economic evaluation, and the cost of PCV were identified as the leading causes of the slow uptake of PCVs in MICs. Potential solutions mentioned in the reviewed papers include the use of vaccine cost-effectiveness analysis and the provision of economic evidence to strengthen decision-making, the evaluation of the burden of disease, and post-introduction surveillance to monitor vaccine impact.
Conclusion: The global community needs to recognise the impediments to vaccine introduction into MICs. Improving PCV access could help decrease the incidence of pneumonia and reduce the selection pressure for pneumococcal antimicrobial resistance.

Keywords: Immunisation, *Streptococcus pneumoniae*, pneumonia, pneumococcal vaccines, middle-income countries, GAVI, health policy.

Ablation IL-33 gene exacerbate myocardial remodeling in mice with heart failure induced by mechanical stress

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Abstract

Background and purpose: ST2 is one of the interleukin (IL)-1 receptor family members comprising of membrane-bound (ST2L) and soluble (sST2) isoforms. Clinical trials have revealed that serum sST2 levels predict outcome in patient with myocardial infarction or chronic heart failure (HF). Meanwhile, we and others have reported that ablation of ST2 caused exaggerated cardiac remodeling in both ischemic and non-ischemic HF. Here, we tested whether IL-33, the ligand for ST2, protects myocardium against HF induced by mechanical overload using ligand specific knockout (IL-33_/_) mice.

Methods and results: Transverse aortic constriction (TAC)/sham surgery were carried out in both IL-33 and WT-littermates. Echocardiographic measurements were performed at frequent interval during the study period. Heart was harvested for RNA and histological measurements. Following mechanical overload by TAC, myocardial mRNA expressions of Th1 cytokines, such as TNF-a were enhanced in IL-33_/_ mice than in WT mice. After 8-weeks, IL-33_/_ mice exhibited exacerbated left ventricular hypertrophy, increased chamber dilation, reduced fractional shortening, aggravated fibrosis, inflammation, and impaired survival compared with WT littermates. Accordingly, myocardial mRNA expressions of hypertrophic (c-Myc/BNP) molecular markers were also significantly enhanced in IL-33_/_ mice than those in WT mice.

Conclusions: We report for the first time that ablation of IL-33 directly and significantly leads to exacerbate cardiac remodeling with impaired cardiac function and survival upon mechanical stress. These data highlight the cardioprotective role of IL-33/ST2 system in the stressed myocardium and reveal a potential therapeutic role for IL-33 in non-ischemic HF.

Keywords: IL-33, Cardiac remodelling, Hypertrophy, Fibrosis, TAC.

Effects of calcium on the incidence of recurrent colorectal adenomas: A systematic review with meta-analysis and trial sequential analysis of randomized controlled trials

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**Abstract**

**Background:** Protective effects of calcium supplementation against colorectal adenomas have been documented in systematic reviews; however, the results have not been conclusive. Our objective was to update and systematically evaluate the evidence for calcium supplementation taking into consideration the risks of systematic and random error and to GRADE the evidence.

**Methods:** The study comprised a systematic review with meta-analysis and trial sequential analysis (TSA) of randomized controlled trials (RCTs). We searched for RCTs published up until September 2016. Retrieved trials were evaluated using risk of bias. Primary outcome measures were the incidences of any recurrent adenomas and of advanced adenomas. Meta-analytic estimates were calculated with the random-effects model and random errors were evaluated with trial sequential analyses (TSAs).

**Results:** Five randomized trials (2234 patients with a history of adenomas) were included. Two of the 5 trials showed either unclear or high risks of bias in most criteria. Meta-analysis of good quality RCTs suggest a moderate protective effect of calcium supplementation on recurrence of adenomas (relative risk [RR], 0.88 [95% CI 0.79–0.99]); however, its effects on advanced adenomas did not show statistical significance (RR, 1.02 [95% CI 0.67–1.55]). Subgroup analyses demonstrated a greater protective effect on recurrence of adenomas with elemental calcium dose ≥1600mg/day (RR, 0.74 [95% CI 0.56–0.97]) compared to ≤1200 mg/day (RR, 0.84 [95% CI 0.73–0.97]). No major serious adverse events were associated with the use of calcium, but there was an increase in the incidence of hypercalcemia (P=.0095).
TSA indicated a lack of firm evidence for a beneficial effect. Concerns with directness and imprecision rated down the quality of the evidence to “low.”

**Conclusion:** The available good quality RCTs suggests a possible beneficial effect of calcium supplementation on the recurrence of adenomas; however, TSA indicated that the accumulated evidence is still inconclusive. Using GRADE-methodology, we conclude that the quality of evidence is low. Large well-designed randomized trials with low risk of bias are needed.

**Keywords:** calcium, chemoprevention, colorectal adenomas, meta-analysis, randomized controlled trials, systematic review, trial sequential analysis.
Effects of aspirin and non-aspirin nonsteroidal anti-inflammatory drugs on the incidence of recurrent colorectal adenomas: A systematic review with meta-analysis and trial sequential analysis of randomized clinical trials

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Abstract

Background: Beneficial effects of aspirin and non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs) against recurrent colorectal adenomas have been documented in systematic reviews; however, the results have not been conclusive. Uncertainty remains about the appropriate dose of aspirin for adenoma prevention. The persistence of the protective effect of NSAIDs against recurrent adenomas after treatment cessation is yet to be established.

Methods: Our objective was to update and systematically evaluate the evidence for aspirin and other NSAIDs on the incidence of recurrent colorectal adenomas taking into consideration the risks of random error and to appraise the quality of evidence using GRADE (The Grading of Recommendations, Assessment, Development and Evaluation) approach. Retrieved trials were evaluated using Cochrane risk of bias instrument. Meta-analytic estimates were calculated with random-effects model and random errors were evaluated with trial sequential analysis (TSA).

Results: In patients with a previous history of colorectal cancer or adenomas, low-dose aspirin (80–160 mg/day) compared to placebo taken for 2 to 4 years reduces the risk of recurrent colorectal adenomas (relative risk (RR), 0.80 [95% CI (confidence interval), 0.70–0.92]). TSA indicated a firm evidence for this beneficial effect. The evidence indicated moderate GRADE quality. Low-dose aspirin also reduces the recurrence of advanced adenomas (RR, 0.66 [95%
CI, 0.44–0.99)); however, TSA indicated lack of firm evidence for a beneficial effect. High-dose aspirin (300–325 mg/day) did not statistically reduce the recurrent adenomas (RR, 0.90 [95% CI, 0.68–1.18]). Cyclooxygenase-2 (COX-2) inhibitors (e.g. celecoxib 400 mg/day) were associated with a significant decrease in the recurrence of both adenomas (RR, 0.66 [95% CI, 0.59–0.72]) and advanced adenomas (RR, 0.45 [95% CI, 0.33–0.57]); however, this association did not persist and there was a trend of an increased risk of recurrent adenomas observed 2 years after the withdrawal.

**Conclusion:** Our findings confirm the beneficial effect of low-dose aspirin on recurrence of any adenomas; however, effect on advanced adenomas was inconclusive. COX-2 inhibitors seem to be more effective in preventing recurrence of adenomas; however, there was a trend of an increased risk of recurrence of adenomas observed after discontinuing regular use.

**Keywords:** Colorectal adenomas, Aspirin, Anti-inflammatory agents, Non-steroidal, Systematic review, Meta-analysis, Randomized controlled trials, Trial sequential analysis.
Effects of chemopreventive agents on the incidence of recurrent colorectal adenomas: a systematic review with network meta-analysis of randomized controlled trials

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Abstract

Background: Protective effects of several chemopreventive agents (CPAs) against colorectal adenomas have been well documented in randomized controlled trials (RCTs); however, there is uncertainty regarding which agents are the most effective.

Methods: We searched for RCTs published up until September 2016. Retrieved trials were evaluated using risk of bias. We performed both pairwise analysis and network meta-analysis (NMA) of RCTs to compare the effects of CPAs on the recurrence of colorectal adenomas (primary outcome). Using NMA, we ranked CPAs based on efficacy.

Results: We identified 20 eligible RCTs enrolling 12,625 participants with a history of colorectal cancer or adenomas who were randomly assigned to receive either a placebo or one of 12 interventions. NMA using all trials demonstrated that celecoxib 800 mg/day (relative risk [RR] 0.61, 95% confidence interval [CI] 0.45–0.83), celecoxib 400 mg/day (RR 0.70, 95% CI 0.55–0.87), low-dose aspirin (RR 0.75, 95% CI 0.59–0.96) and calcium (RR 0.81, 95% CI 0.69–0.96) were significantly associated with a reduction in the recurrence of any adenomas. NMA results were consistent with those from pairwise meta-analysis. The evidence indicated
a high (celecoxib), moderate (low-dose aspirin) and low (calcium) Grading of Recommendations, Assessment, Development and Evaluation (GRADE) quality. NMA ranking showed that celecoxib 800 mg/day and celecoxib 400 mg/day were the best CPAs, followed by low-dose aspirin and calcium. Considering advanced adenoma recurrence, only celecoxib 800 mg/day and celecoxib 400 mg/day were demonstrated to have a protective effect (RR 0.37, 95% CI 0.27–0.52 vs RR 0.48, 95% CI 0.38–0.60, respectively).

**Conclusion:** The available evidence from NMA suggests that celecoxib is more effective in reducing the risk of recurrence of colorectal adenomas, followed by low-dose aspirin and calcium. Since cyclooxygenase-2 (COX-2) inhibitors (eg, celecoxib) are associated with important cardiovascular events and gastrointestinal harms, more attention is warranted toward CPAs with a favorable benefit-to-risk ratio, such as low-dose aspirin and calcium.

**Keywords:** colorectal adenomas, chemoprevention, systematic review, meta-analysis, network meta-analysis, randomized controlled trials.
Uncovering a protease in snake venom capable to coagulate milk to curd

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Abstract
Snake venom been studied for its lethality and various benefits for mankind. The latter been studied a plenty of recent but none related to coagulation of milk to curd. The coagulation time of milk by samples were done using visible parameters i.e. change in viscosity, colour changes, white spot formation (separation between curd and whey) and finally observing a drop of coagulating fluid under magnification of a light microscope. Optimum parameters determined included concentration of coagulants, temperature and pH. Microscopic viewing included observing after centrifugation, under light microscope and SEM. Screening eleven venoms mostly predominantly found in tropical region singled out one with the most rapid coagulating time i.e by Calloselasmarhodostoma (CR). Optimization of CR venom related to several parameters provided venom concentration, 0.07 (w/v%); pH,7.0; temperature, 45.50°C while that of rennet were determined to be 0.04±0.02 (w/v%); pH,7.0; temperature, 45.50°C, respectively. Under these ideal conditions for both coagulants, comparison of their milk coagulation time found CR superior i.e. 0.41±0.02 min compared to 4.23±0.05 min for rennet. Milk coagulating assay guided fractionation of CR venom by using HiTrap SP FF and consecutively followed by HiPrep 26/60 Sephacryl S200 HR pre-packed columns led to a single band on coomassie stained SDS-PAGE gel. Next by LCMS analysis on the SDS PAGE band identified the presence of metalloproteinase kistomin within the venom. EDTA inactivated the venom presumably chelating zinc hence suggesting further towards identifying kistomin as the likely protease within this venom with milk-clotting activity. Snake venom been potentially identified for yet another application for the benefit of mankind. In this investigation Malayan Pit Viper’s protease can play major role in dairy industry if studied further.

Keywords: Coagulation, protease, dairy, snake, protein, curd.
Susceptibility of human oral squamous cell carcinoma (OSCC) H103 and H376 cell lines to retroviral OSKM mediated reprogramming

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Abstract

Although numbers of cancer cell lines have been shown to be successfully reprogrammed into induced pluripotent stem cells (iPSCs), reprogramming Oral Squamous Cell Carcinoma (OSCC) to pluripotency in relation to its cancer cell type and the expression pattern of pluripotent genes under later passage remain unexplored. In our study, we reprogrammed and characterised H103 and H376 oral squamous carcinoma cells using retroviral OSKM mediated method. Reprogrammed cells were characterized for their embryonic stem cells (ESCs) like morphology, pluripotent gene expression via quantitative real-time polymerase chain reaction (RT-qPCR), immunofluorescence staining, embryoid bodies (EB) formation and directed differentiation capacity. Reprogrammed H103 (Rep-H103) exhibited similar ESCs morphologies with flatten cells and clear borders on feeder layer. Reprogrammed H376 (Rep-H376) did not show ESCs morphologies but grow with a disorganized morphology. Critical pluripotency genes Oct4, Sox2 and Nanog were expressed higher in Rep-H103 against the parental counterpart from passage 5 to passage 10. As for Rep-H376, Nanog expression against its parental counterpart showed a significant decrease at passage 5 and although increased in passage 10, the level of expression was similar to the parental cells. Rep-H103 exhibited pluripotent signals (Oct4, Sox2, Nanog and Tra-1-60) and could form EB with the presence of three germ layers markers. Rep-H103 displayed differentiation capacity into adipocytes and osteocytes. The OSCC cell line H103 which was able to be reprogrammed into an iPSC like state showed high expression of Oct4, Sox2 and Nanog at late passage and may provide a potential iPSC model to study multi-stage oncogenesis in OSCC.

Keywords: Oral Squamous Cell Carcinoma, Reprogramming, Cancer cells, Induced pluripotent stem cells, Differentiation capacity, Pluripotency, Embryonic stem cells.

Safe zone in anterior mandible related to the genial tubercle for implant osteotomy in a Chinese-Malaysian population: A CBCT study

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Abstract

Statement of Problem: The genial tubercle is a clinically palpable landmark in the mandible and can be identified in cone beam computed tomography (CBCT). Its location can be used to measure the safe zone in the interforaminal region of the mandible. These measurements may be helpful for implant treatment planning in patients with complete edentulism.

Purpose: The purpose of this clinical study was to evaluate the safe distance in the interforaminal region of the mandible measured from the genial tubercle level for implant osteotomy in a Chinese-Malaysian population.

Material and Methods: A total of 201 Digital Imaging and Communications in Medicine (DICOM) files were selected for the study from the CBCTs of dentate or edentulous Chinese-Malaysian adult patients with ongoing or completed treatments. Measurements were made with implant planning software. The anatomy of the whole mandible was assessed in the coronal cross-sectional, horizontal view and in panoramic view. Measurements were obtained in millimeters on one side by locating and marking a genial tubercle and then marking the mesial margin of the mental foramen and the anterior loop of the inferior alveolar nerve. The corresponding points of these landmarks were identified on the crest of the mandibular ridge to measure the linear distances. All the measurement steps were repeated on the other side. The linear distance of 2 mm was deducted from the total distance between the genial tubercle and the anterior loop separately for left and right side measurements to identify the safe zone. The mixed 2-way analysis of variance (ANOVA) test was used to analyze side and sex-related variations.

Results: The mean safe zone measured at the crestal level from the genial tubercle site on the left side of the mandible was 21.12 mm and 21.67 mm on the right side. A statistically significant (P<.05) difference was found between the left and right sides of the safe zone measurements in both men and women. No statistically significant differences were found in the safe zone between men and women on either the left or right side (P=.655). The minimum distance from the genial tubercle to the right side safe zone in women was 12.82 mm and 14.99 mm in men; however, on the left side, the minimum distance was observed to be 14.81 mm in women and 15.54 mm in men.

Conclusions: The safe zone related to the genial tubercle was 21.12 mm on the left side and 21.67 mm on the right side, with no significant sex-related variations. Within the same individuals, a significant difference was found in the safe zone between the left and right side.
Repurposing pentoxifylline for the treatment of fibrosis: An overview

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Abstract

Fibrosis is a potentially debilitating disease with high morbidity rates. It is estimated that half of all deaths that occur in the USA are attributed to fibrotic disorders. Fibrotic disorders are characterized primarily by disruption in the extracellular matrix deposition and breakdown equilibrium, leading to the accumulation of excessive amounts of extracellular matrix. Given the potentially high prevalence of fibrosis and the paucity of agents currently available for the treatment of this disease, there is an urgent need for the identification of drugs that can be utilized to treat the disease. Pentoxifylline is a methylxanthine derivative that is currently approved for the treatment of vascular diseases, in particular, claudication. Pentoxifylline has three main properties: improving the rheological properties of blood, anti-inflammatory, and antioxidative. Recently, the effectiveness of pentoxifylline in the treatment of fibrosis via attenuating and reversing fibrotic lesions has been demonstrated in several clinical trials and animal studies. As a result of the limited availability of antifibrotic agents in the long-term treatment of fibrosis that can attenuate and even reverse fibrotic lesions effectively, it would be of particular importance to consider the potential clinical utility of pentoxifylline in the treatment of fibrosis. Thus, this paper discusses the evolving roles of pentoxifylline in the treatment of different types of fibrosis.

Keywords: Drug repurposing, Fibrosis, Pentoxifylline, Pharmacology.
Neonatal alloimmune thrombocytopenia associated with maternal HLA antibodies

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Abstract
Neonatal alloimmune thrombocytopenia (NAIT) generally results from platelet opsonisation by maternal antibodies against fetal platelet antigens inherited from the infant’s father. Newborn monochorionic twins presented with petechial haemorrhages at 10 hours of life, along with severe thrombocytopenia. Despite the initial treatment with platelet transfusions and intravenous immunoglobulin, they both had persistent thrombocytopenia during their first 45 days of life. Class I human leucocyte antigen (HLA) antibodies with broad specificity against several HLA-B antigens were detected in the maternal serum. Weak antibodies against HLA-B57 and HLA-B58 in sera from both twins supported NAIT as the most likely diagnosis. Platelet transfusion requirements of the twins lasted for 7 weeks. Transfusion of HLA-matched platelet concentrates was more efficacious to manage thrombocytopenia compared with platelet concentrates from random donors. Platelet genotyping and determination of HLA antibody specificity are needed to select compatible platelet units to expedite safe recovery from thrombocytopenia in NAIT.

**Recent advances in hyaluronic acid-decorated nanocarriers for targeted cancer therapy**

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**Abstract**

The cluster-determinant 44 (CD44) receptor has a high affinity for hyaluronic acid (HA) binding and is a desirable receptor for active targeting based on its overexpression in cancer cells compared with normal body cells. The nanocarrier affinity can be increased by conjugating drug-loaded carriers with HA, allowing enhanced cancer cell uptake via the HA–CD44 receptor-mediated endocytosis pathway. In this review, we discuss recent advances in HA-based nanocarriers and micelles for cancer therapy. In vitro and in vivo experiments have repeatedly indicated HA-based nanocarriers to be a target-specific drug and gene delivery platform with great promise for future applications in clinical cancer therapy.
Win TT, Othman NH, Mohamad I. Poorly differentiated thyroid carcinoma: A hospital-based clinicopathological study and review of literature. Indian Journal of Pathology and Microbiology, 2017; 60(2): 167-171. Doi: 10.4103/IJPM.IJPM_457_16. (ISI IF: 0.616; CiteScore: 0.55; Tier: Q3).

Poorly differentiated thyroid carcinoma: A hospital-based clinicopathological study and review of literature

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Abstract
Introduction: Poorly differentiated thyroid carcinoma (PDTC) is a rare aggressive malignancy of thyroid follicular cells and has unique features in morphology and behavior. This study was aimed to describe the experience of a tertiary medical center with PDTC within a 10-year period.

Materials and Methods: This is a descriptive retrospective study of eight cases of PDTC among 418 various thyroid carcinomas. All cases of PDTC were retrieved along with the clinicopathological information.

Results: Only eight cases (1.9%) of PDTC were diagnosed among 418 thyroid carcinomas. Mean age was 48.12 with 3:5 (male:female) and tumor size ranged 3–12 cm. PDTC were diagnosed coexisting with one or more other pathologies; nodular hyperplasia (four cases), papillary carcinoma (one case), follicular carcinoma (three cases), and Hashimoto thyroiditis (two cases); with ≥60% PDTC component. Six cases associated with high-grade features died within 3 years after diagnosis. Discussion: Mean age in this study was younger including a 20-year-old girl. Younger age was associated with better prognosis. Most of the cases had underlying benign thyroid lesions and differentiated thyroid carcinoma. Most of the PDTC had poor prognosis associated with PDTC component ≥60%, tumor necrosis, high mitotic count, lymph node involvement, vascular invasion and distant metastasis; and these cases died within 3 years after diagnosis.

Conclusion: Although treatment of PDTC remains surgery followed by radioiodine therapy, correct histopathological diagnosis is important for clinicians and oncologists to predict the prognosis. All thyroid carcinoma should be sampled thoroughly not to miss small foci of PDTC component.

Keywords: Poorly differentiated thyroid carcinoma, thyroid carcinomas, clinicopathological correlation, Turin.
Abstract
E-cadherin is a transmembrane glycoprotein which connects epithelial cells together at adherens junctions. In normal cells, E-cadherin exerts its tumour suppressing role mainly by sequestering β-catenin from its binding to LEF (Lymphoid enhancer factor)/TCF (T cell factor) which serves the function of transcribing genes of the proliferative Wnt signaling pathway. Despite the ongoing debate on whether the loss of E-cadherin is the cause or effect of epithelial-mesenchymal transition (EMT), E-cadherin functional loss has frequently been associated with poor prognosis and survival in patients of various cancers. The dysregulation of E-cadherin expression that leads to carcinogenesis happens mostly at the epigenetic level but there are cases of genetic alterations as well. E-cadherin expression has been linked to the cellular functions of invasiveness reduction, growth inhibition, apoptosis, cell cycle arrest and differentiation. Studies on various cancers have shown that these different cellular functions are also interdependent. Recent studies have reported a rapid expansion of E-cadherin clinical relevance in various cancers. This review article summarises the multifaceted effect E-cadherin expression has on cellular functions in the context of carcinogenesis as well as its clinical implications in diagnosis, prognosis and therapeutics.

Keywords: E-cadherin, Dysregulation, Invasiveness, Apoptosis, Carcinogenesis.

**Effects of 25-hydroxyvitamin D and vitamin D-binding protein on bone mineral density and disease activity in Malaysian patients with rheumatoid arthritis**

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**Abstract**

**Aim:** Vitamin D3 [25(OH)D] has been shown to be important in bone health and can influence rheumatoid arthritis (RA) disease activity. Vitamin D-binding protein (VDBP) levels vary with race and may modulate 'bioavailable' levels of 25(OH)D. The aim of this study was to explore the relationships between 25(OH)D, VDBP and clinical factors on bone mineral density (BMD) in a group of multi-ethnic Malaysian RA patients and healthy controls.

**Methods:** A cross-sectional study of 77 female RA patients and 29 controls was performed. Serum 25(OH)D was measured using the Elecsys Vitamin D total assay. Serum VDBP was measured using a Quantikine enzyme-linked immunosorbent assay kit. BMD was assessed using dual-energy X-ray absorptiometry (DXA).

**Results:** Overall, mean 25(OH)D levels were 42.66 ± 21.75 nmol/L with no significant difference between RA patients and controls. 25(OH)D levels were significantly higher in Chinese, compared to Malay/Indian subjects. In RA patients, menopausal status and body mass index (BMI) were significantly associated with BMD but not 25(OH)D or RA Disease Activity Score of 28 joints (DAS28). There was no significant correlation between 25(OH)D and DAS28, even after correction for menopausal status and BMI. VDBP levels were not significantly different between the races and did not significantly correlate with BMD, 25(OH)D overall, or DAS28 in RA patients.

**Conclusions:** In Malaysian RA patients, menopausal status and BMI were more important influences on BMD than 25(OH)D or RA disease activity. The utility of measuring VDBP levels in this population remains uncertain.

**Keywords:** 25hydroxyvitamin D3, Asian, DAS28, rheumatoid arthritis, vitamin D binding protein.
Biocompatible palm stearin-based polyesteramide as polymer carrier for solid dispersion

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Abstract
Palm stearin-based polyesteramide (PSPEA) was synthesized by reacting PS with diethanolamine, followed by azelaic acid at functionality molar ratio (OH: COOH) ranged 1:0.84 to 1:0.95 at 150–190 °C. FTIR, 1H-nuclear magnetic resonance, 13C-nuclear magnetic resonance, and gel permeation chromatography were used to elucidate the chemical structure and $M_w$ distribution of the PSPEA. PSPEA 4000 (acid value = 0.61 mg KOH/g sample, hydroxyl value = 51.97 mg KOH/g sample) was used in combination with stearic acid-based PEA to prepare mefenamic acid (MA) solid dispersion. The solid dispersion demonstrated sixfold and twofold enhancement in $T_{50%}$ and cumulative drug release as compared to pure MA. The differential scanning calorimetry and scanning electron microscopy analyses revealed solubilization of MA in PEA and transformation of MA into amorphous. In vitro cytotoxicity studies confirmed the safety profile of PSPEA against 3T3 fibroblast cell lines. This work demonstrated that the biocompatible PSPEA possesses surface tension lowering and anticrystallization effects have the potential as polymer carrier for pharmaceutical dosage forms.
Preparation and evaluation of palm oil-based polyesteramide solid dispersion for obtaining improved and targeted dissolution of mefenamic acid

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Abstract

Purpose: The aim of this work was to investigate the functional role of newly synthesised palm oil-based polyesteramide (POPEA) and stearic acid-based polyesteramide (SAPEA) in mefenamic acid (MA) solid dispersion (SD).

Methods: Solid dispersions of MA were prepared by hot melt method, using a combination of POPEA/SAPEA as a polymer carrier. The effects of POPEA/SAPEA mixture ratio, drug loading percentage and influence of different Mw of POPEA (4000–17,000 Da) in SD were investigated. The SDs were characterised for drug content, solubility, dissolution behaviour and physico-chemical characteristics by DSC and FTIR. Comparisons were made with pure drug, physical mixture and a marketed MA formulation.

Results: All SDs demonstrated faster dissolution rate than pure MA and SD 6 formulated with SAPEA/POPEA 4000 Da, 8:2 showed the highest T50 release rate (45 min) with no significant difference (P > 0.05) compared to marketed formulation. All SDs showed improved drug release (85.48 ± 1.17 to 90.66 ± 1.53%) against marketed formulation (81.30 ± 1.26%) and MA (56.27 ± 1.08%) after 6 h of dissolution. DSC endothermic peak for MA in SD 6 was broadened and shifted to lower temperature (194 °C). FTIR spectroscopy confirmed no chemical changes in MA SD, but establishment of hydrogen bonding between hydroxyl groups of PEA with amine groups of MA was observed by the red shift of OH band in SD samples. The SD was stable (P > 0.05) at ambient condition for up to 90 days, reflecting by the drug content, dissolution profiles and solubility of the formulation.

Conclusions: POPEA demonstrated surface lowering and wettability effects in improving the aqueous solubility and dissolution rate of MA in SD. The crystalline drug was transformed to amorphous formulation, via solubilisation and crystallisation inhibition effect of the PEA.

Keywords: Palm oil-based polyesteramide, Solid dispersion, Dissolution, Solubility, Mefenamic acid, Stability.
Molecular understanding of the protective role of natural products on isoproterenol-induced myocardial infarction: A review

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Abstract
Modern medicine has been used to treat myocardial infarction, a subset of cardiovascular diseases, and have been relatively effective but not without adverse effects. Consequently, this issue has stimulated interest in the use of natural products, which may be equally effective and better tolerated. Many studies have investigated the cardioprotective effect of natural products, such as plant-derived phytochemicals, against isoproterenol (ISO)-induced myocardial damage; these have produced promising results on the basis of their antioxidant, anti-atherosclerotic, anti-apoptotic and anti-inflammatory activities. This review briefly introduces the pathophysiology of myocardial infarction (MI) and then addresses the progress of natural product research towards its treatment. We highlight the promising applications and mechanisms of action of plant extracts, phytochemicals and polyherbal formulations towards the treatment of ISO-induced myocardial damage. Most of the products displayed elevated antioxidant levels with decreased oxidative stress and lipid peroxidation, along with restoration of ionic balance and lowered expression of myocardial injury markers, pro-inflammatory cytokines, and apoptotic parameters. Likewise, lipid profiles were positively altered and histopathological improvements could be seen from, for example, the better membrane integrity, decreased necrosis, edema, infarct size, and leukocyte infiltration. This review highlights promising results towards the amelioration of ISO-induced myocardial damage, which suggest the direction for future research on natural products that could be used to treat MI.

Keywords: Cardiovascular, Antioxidant, Myocardial infarction, Phytochemicals, Isoproterenol.

**Additivity vs synergism: Investigation of the additive interaction of cinnamon bark oil and meropenem in combinatory therapy**

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**Abstract**

Combinatory therapies have been commonly applied in the clinical setting to tackle multi-drug resistant bacterial infections and these have frequently proven to be effective. Specifically, combinatory therapies resulting in synergistic interactions between antibiotics and adjuvant have been the main focus due to their effectiveness, sidelining the effects of additivity, which also lowers the minimal effective dosage of either antimicrobial agent. Thus, this study was undertaken to look at the effects of additivity between essential oils and antibiotic, via the use of cinnamon bark essential oil (CBO) and meropenem as a model for additivity. Comparisons between synergistic and additive interaction of CBO were performed in terms of the ability of CBO to disrupt bacterial membrane, via zeta potential measurement, outer membrane permeability assay and scanning electron microscopy. It has been found that the additivity interaction between CBO and meropenem showed similar membrane disruption ability when compared to those synergistic combinations which was previously reported. Hence, results based on our studies strongly suggest that additive interaction acts on a par with synergistic interaction. Therefore, further investigation in additive interaction between antibiotics and adjuvant should be performed for a more in depth understanding of the mechanism and the impacts of such interaction.

**Keywords:** additive interaction, antibiotic resistance, cinnamon bark essential oil, combinatory treatment, membrane disruption.

**Body weight status and dietary intakes of urban Malay primary school children: Evidence from the Family Diet Study**

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**Abstract**

Malaysia is experiencing a rise in the prevalence of childhood obesity. Evidence for the relationship between dietary intake and body weight among Malaysian children is limited, with the impact of energy intake misreporting rarely being considered. This paper describes the dietary intakes of urban Malay children in comparison to national recommendations and by weight status. This cross-sectional Family Diet Study (n = 236) was conducted in five national primary schools in Malaysia (August 2013–October 2014). Data on socio-demographics, anthropometrics, 24-h dietary recalls, and food habits were collected from Malay families, consisting of a child aged 8 to 12 years and their main caregiver(s). Multivariable analyses were used to assess dietary intake-body weight relationships. The plausibility of energy intake was determined using the Black and Cole method. Approximately three in 10 Malay children were found to be overweight or obese. The majority reported dietary intakes less than national recommendations. Children with obesity had the lowest energy intakes relative to body weight (kcal/kg) compared to children in other weight categories (F = 36.21, p < 0.001). A positive moderate correlation between energy intake and weight status was identified (r = 0.53, p < 0.001) after excluding energy intake mis-reporters (n = 95), highlighting the need for the validation of dietary assessment in obesity-related dietary research in Malaysia.

**Keywords:** child; diet; nutrition; body weight; energy misreporting; developing country.

**Enhanced marine antifouling performance of silver-titania nanotube composites from hydrothermal processing**

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**Abstract**

Marine fouling is an age-old problem which continues to plague the maritime industry. The fouling process progresses from an initial formation of bacterial biofilm on unprotected surfaces. Silver is a well-known antimicrobial agent which is well-tolerated by mammals, while titania nanotubes have enhanced properties due to a greater specific surface area on the inner and outer surfaces of the tubular structure. A novel 2-step hydrothermal synthesis of a silver-titania nanotube (Ag/TNT) composite material is presented. The morphology, particle size, chemical content, crystal structure, optical properties and surface area were systematically characterized. Determination of biofilm inhibitory properties revealed that Ag/TNT with the lowest silver content (0.95 wt% Ag) decorated with Ag nanoparticles of ca. 3 nm reduced biofilm formation of marine bacterium *Halomonas pacifica* by 98% compared to pure titania nanotubes and bulk silver alone. Growth inhibition of marine microalgae *Dunaliella tertiolecta* and *Isochrysis* sp. were also observed.

**Contrasting sirtuin and PARP activity of selected 2,4,6-trisubstituted benzimidazoles**

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**Abstract**

Both sirtuin and poly(ADP-ribose)polymerase (PARP) family of enzymes utilize NAD+ as co-substrate. Inhibitors of sirtuins and PARPs are important tools in drug discovery as they are reported to be linked to multiple diseases such as cancer. New potent sirtuin inhibitors (2,4,6-trisubstituted benzimidazole) were discovered from reported PARP inhibitor scaffold. Interestingly, the synthesized compounds have contrasting sirtuin and PARP-1 inhibitory activities. We showed that modification on benzimidazoles may alter their selectivity toward sirtuin or PARP-1 enzymes. This offers an opportunity for further discovery and development of new promising sirtuin inhibitors. Molecular docking studies were carried out to aid the rationalization of these observations. Preliminary antiproliferative studies of selected compounds against nasopharyngeal cancer cells also showed relatively promising results.

**Keywords:** anticancer, benzo[d]imidazole, molecular docking, nasopharyngeal, poly(ADP-ribose) polymerases, sirtuin.

**Social and communicative functions of informed consent forms in East Asia and beyond**

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**Abstract**

The recent research and technology development in medical genomics has raised new issues that are profoundly different from those encountered in traditional clinical research for which informed consent was developed. Global initiatives for international collaboration and public participation in genomics research now face an increasing demand for new forms of informed consent which reflect local contexts. This article analyzes informed consent forms (ICFs) for genomic research formulated by four selected research programs and institutes in East Asia – the Medical Genome Science Program in Japan, Universiti Sains Malaysia Human Research Ethics Committee in Malaysia, and the Taiwan Biobank and the Taipei Medical University-Joint Institutional Review Board in Taiwan. The comparative text analysis highlights East Asian contexts as distinct from other regions by identifying communicative and social functions of consent forms. The communicative functions include re-contact options and offering interactive support for research participants, and setting opportunities for family or community engagement in the consent process. This implies that informed consent cannot be validated solely with the completion of a consent form at the initial stage of the research, and informed consent templates can facilitate interactions between researchers and participants through (even before and after) the research process. The social functions consist of informing participants of possible social risks that include genetic discrimination, sample and data sharing, and highlighting the role of ethics committees. Although international ethics harmonization and the subsequent coordination of consent forms may be necessary to maintain the quality and consistency of consent process for data-intensive international research, it is also worth paying more attention to the local values and different settings that exist where research participants are situated for research in medical genomics. More than simply tools to gain consent from research participants, ICFs function rather as a device of social communication between research communities and civic communities in liaison with intermediary agents like ethics committees, genetic counselors, and public biobanks and databases.

**Keywords:** medical genomics, consent documents, group consent, family consent, community engagement.

**Investigation on secondary structure perturbations of proteins embedded in solid lipid matrices as a novel indicator of their biological activity upon in vitro release**

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**Abstract**

Protein biologics are prone to conformational changes during formulation development. Limited methods are available for conformational analysis of proteins in solid state and in the presence of formulation excipients. The aim of this study was to investigate the secondary structures of proteins encased in solid lipid matrices as a novel indicator of their stability upon in vitro release. Model proteins namely catalase and lysozyme were incorporated into lipid namely Precirol® AT05 (glycerol palmitostearate, melting point 58°C) at 30% w/w loading using melting and mixing and wet granulation methods. Attenuated total reflectance (ATR-FTIR) spectroscopy, size-exclusion chromatography (SEC) and biological activity analyses were performed. The information about secondary structure was acquired using second derivative analysis of amide-I band (1600-1700 cm\(^{-1}\)). ATR analysis demonstrated interference of lipid spectrum with protein amide-I band which was subsequently subtracted to allow the analysis of the secondary structure. ATR spectra amide-I bands showed shifts in peak band positions compared to native protein for matrices prepared using wet granulation. SEC analysis gave evidence of protein aggregation for catalase which was increased using wet granulation. The biological activity of catalase was statistically different from that of control and was affected by the incorporation method and was found to be in alignment with ATR spectral changes and extent of aggregation. In conclusion, ATR spectroscopy could analyze protein secondary structure in lipid matrices provided lipid interference was minimized. The ATR spectral changes and formation of aggregates can indicate the loss in biological activity of protein released from solid lipid matrices.

**Keywords:** ATR spectroscopy, Biological activity, Lipid matrices, Proteins, Size-exclusion chromatography.